INTERNATIONAL ABSTRACTS OF SURGERY

VOLUME 91 OCTOBER, 1950 NUMBER 4

COLLECTIVE REVIEW

PRINCIPLES AND TECHNIQUES OF PROTEIN THERAPY IN SURGICAL PATIENTS

JAMESON L. CHASSIN, M.D., New York, N. Y.

DURING the past decade surgeons have come to recognize that the state of the patient's protein nutrition is a vital factor in deciding the success or failure of a major operation (211, 217). That numerous complications (Table II) follow in the train of protein depletion has been thoroughly emphasized (71, 108, 143, 178). On the other hand, the principles and techniques of protein repletion therapy have been surrounded by confusion and controversy. Where one group (217) recommends whole protein concentrates perorally, another (52, 55) uses huge doses of protein hydrolysates by mouth. Lyons and his associates (47) emphasize massive replacement therapy with whole blood transfusions, and Elman (71, 72) gives 2 liters of protein hydrolysate a day intravenously as a routine measure.

In the light of these differences among the authorities in this field, it is not surprising that many misconceptions have arisen in the minds of the surgical practitioner. Among the more common of these erroneous beliefs are the following: (1) a total serum protein concentration of 6.0 grams per cent or higher rules out protein deficiency; (2) a dose of 1 gram of protein per kilogram of body weight per day is adequate for repletion therapy; (3) caloric requirements may be generally ignored in outlining a course of parenteral protein therapy; (4) daily administration of 2 liters of 5 per cent parenteral protein hydrolysate in 5 per cent dextrose solution insures the adequacy of repletion therapy; and (5) blood or plasma transfusion alone constitutes good treatment for hypoproteinemia.

The prevalence of these misconceptions has become evident to us while presenting the subject of protein metabolism to matriculates in postgraduate courses for surgeons. For this reason the attempt has been made to evaluate critically the various therapeutic agents (blood, plasma, human albumin, protein hydrolysate, whole protein concentrates) and their respective routes of administration (oral, jejunal, parenteral). From a review of the basic literature certain facts have become apparent and these we have tried to synthesize into a rational program of replacement therapy consistent with the present body of scientific evidence yet practical and applicable to surgical practice.

DETECTION OF HYPOPROTEINISM[1]

Whipple (149) has demonstrated that a state of equilibrium exists between the serum protein and the protein of the tissues. Nevertheless, the

From the Post-Graduate Medical School of the New York University-Bellevue Medical Center and the Fourth Surgical Division of Bellevue Hospital.

[1]A term coined to convey the general concept of protein depletion (137). "Hypoproteinemia" should be used only to designate a subnormal concentration specifically of the blood proteins. Since protein depletion can exist without diminished serum protein concentration as tested by present clinical methods, there is need for a more general term to denote depletion of the proteins of the tissue or of the blood or both.

finding of a "normal" serum protein concentration does not rule out a serious degree of protein depletion for several reasons:

1. Depleted patients may suffer some degree of dehydration or contraction of the plasma volume (47, 157) with a concomitant tendency toward hemoconcentration. This obviously would serve to mask a low serum protein concentration.

2. It must be remembered that it is primarily the albumin fraction which reflects protein deficiency (43, 223). The globulins may be increased even in the presence of hypoproteinemia, thereby giving a deceptively high total serum protein concentration (157).

3. Since normal serum protein and albumin concentrations have been shown to occur after prolonged periods of semistarvation (104, 122), it is possible that the body attempts under certain conditions to bolster the serum proteins at the expense of tissue proteins (54, 178).

4. The routine chemical methods of determining the serum protein, especially the albumin levels, are subject to a significant range of error.

With emphasis on the practical limitations of blood protein concentration as a gauge of hypoproteinism, studies from this laboratory have demonstrated a diminished protein concentration in the rectus fascia of 17 patients who suffered postoperative wound disruption; yet 13 of these patients had serum protein concentrations of 6.1 grams per cent or higher (137). Others (11) have noted "that the ease with which the normal plasma protein concentration was restored seemed more closely related to the extent of the starvation period than to the pretransfusion plasma protein concentration."

The clinical history and appearance of the patient should therefore receive close attention in the evaluation of the protein depletion. Unexplained weight loss in a nonobese person means protein loss. Certain conditions, listed in Table I, are almost synonymous with protein depletion and should be treated as such even if the serum protein concentrations appear to be normal.

Although a normal serum protein concentration does not indicate normal protein nutrition, a subnormal serum protein level is good evidence of hypoproteinism. Normal values by the usual clinical methods are: total serum proteins, from 6.3 to 8.0 grams per cent and serum albumin, from 3.9 to 5.3 grams per cent (157). In order to increase the value of these determinations, it has been recommended (157) that plasma volume studies be done routinely in combination with the serum protein determination so as to measure the total circulating plasma protein rather than the protein content per 100 cubic centimeters of plasma. Beling and his associates go so far as to recommend quantitative calculation of the degree of depletion on the basis of the plasma protein deficit. Actually, this procedure is impractical. Gibson and Evans (90) and Griffin *et al.*, employing a method of measuring plasma volume which is more accurate than the one used by Beling, found a wide range of values for plasma volume as related to weight, height, or surface area in *normal* individuals. In particular, after a study of 77 normal determinations, it was found that the total circulating protein or albumin per kilogram of body weight showed too wide a latitude of normal variation to be of any value as a gauge of protein depletion (97). Henschel and his coworkers and Co Tui (54) found that the plasma volume was often above normal in depleted patients. The total circulating serum protein and albumin per kilogram of body weight seemed also to be above normal in the majority of the 26 depleted patients studied (54).

Furthermore, it has been our experience that the standard 10 minute plasma volume method (96) may give inaccurate and inconsistent results when compared with the more cumbersome dye disappearance curve method of Gibson and Evans (90). There is certainly not sufficient evidence at this time to recommend its use as a routine clinical procedure for determining the magnitude of protein deficiency in surgical patients. Chief reliance must be placed upon the history and nature of the disease and the clinical appearance of the patient, and laboratory tests should be used only as secondary adjuncts in evaluating protein depletion.

PATHOLOGICAL PHYSIOLOGY OF HYPOPROTEINISM

Whereas fat can be synthesized from carbohydrate and carbohydrate from protein, the animal organism cannot fabricate protein from any class of food other than protein itself or its digestion products, the peptides and amino acids. Although certain keto-acids may be converted into amino acids (216), this process probably does not account for any significant fraction of the total body protein metabolism. From the amino acids the body derives the specialized proteins of enzymes, hormones, hemoglobin, antibodies, and of protoplasm itself. The plasma protein, especially the albumin fraction, provides the osmotic pressure which maintains the integrity of the plasma fluid compartment. When the serum albumin falls below the "critical level" of 2.5 grams per cent, edema usually develops (167).

In the normal adult there is a precise balance between the intake of protein nitrogen and the output of nitrogenous breakdown products such as urea, ammonia, and creatinine. These are excreted primarily in the urine. This equilibrium between the anabolism and catabolism of proteins is termed "nitrogen balance." Positive nitrogen balance or nitrogen retention constitutes indirect evidence of new tissue protein synthesis in the form of cellular protoplasm, plasma protein, and hemoglobin. Such a situation occurs during the years of body growth and also during proper repletion therapy. Negative nitrogen balance with breakdown of body tissue proteins occurs during episodes of inadequate dietary intake, infectious disease (98), and following operations (60).

Tissue protein breakdown also occurs when the patient receives an insufficient number of calories even though the minimal protein requirement may be present in the diet (207). In this case either dietary or tissue protein or both are deaminated and converted into glucose by the liver ("gluconeogenesis"). This glucose then undergoes combustion to satisfy the energy requirement, and the wasted nitrogen is excreted as urea. Protein breakdown caused by caloric insufficiency may be inhibited by including greater quantities of carbohydrate and fat in the diet (200). This is termed the "protein-sparing" property of glucose and fat. The organism cannot overcome important shortages of energy-producing foodstuffs solely by utilizing its own fat and glycogen depots. Apparently, under such conditions a certain amount of tissue protein must also be sacrificed (85).

The existence of endogenous reserve stores of protein has been demonstrated by Whipple and his group (149). For example, following rapid experimental plasma depletion a *fasting* dog can re-form from 40 to 60 per cent of the entire mass of plasma protein (149). It has not been possible to localize these protein stores anatomically. Apparently a portion of the cytoplasmic protein of certain tissues is subject to call by the organism for conversion into other forms of protein in response to specific needs (127). As much as 40 per cent of the protein content of the rat's liver is removed during a 7 days' fast (5). Luck has shown that this labile fraction of the liver protein cannot be distinguished chemically from the intrinsic cytoplasm itself. Protein of the liver cell nucleus, on the other hand, cannot be mobilized in this manner (127).

Another important contribution by Whipple (149, 230) is the demonstration that a dynamic equilibrium exists between the protein of the plasma and that of the various tissues. This concept was confirmed by the isotope tracer studies of Shoenheimer who fed rats a single labeled amino acid and soon found the labeled group widely dispersed among the proteins and amino acids of the body, which proved that there is a rapid and continuous interchange among the fractions of the various body proteins. This dynamic equilibrium is of direct clinical importance. For example, if a patient with a serum albumin level of 2.8 grams per cent receives, during a 4 or 5 day period, a quantity of normal plasma sufficient to replace his entire plasma volume (3,000 cubic centimeters), it is usually found that the serum albumin and serum protein levels do not return to normal. The reason for this phenomenon lies in the fact that each gram of circulating plasma protein is in equilibrium with 30 grams of tissue protein. Therefore, it has been postulated that of each 30 grams of transfused plasma protein only 1 gram is utilized for the correction of the plasma protein deficit, while the remainder goes to replenish the tissue protein (194). This is apparently true of retained dietary protein also (12).

The clinical causes and manifestations of hypoproteinism have been reviewed and are listed in Tables I and II. Several points, however, deserve further emphasis. A frequently overlooked manifestation of severe protein deficiency is impairment of liver function (4, 13, 76, 93, 136) with fatty infiltration of the liver (3, 100, 105, 106, 169, 182), which in some cases is severe enough to resemble acute yellow atrophy both clinically and histologically (217). When a patient with this type of liver pathology is subjected to surgery, a fatal hepatic insufficiency may result (179). In the past it was stressed that carbohydrates were essential in the treatment of fatty liver and in preparing jaundiced patients for surgery. However, in recent years it has been shown that normal rats, placed on low protein diets, develop fatty infiltration as well as hepatic cirrhosis and necrosis (106). High protein feeding tends to reduce the degree of fatty infiltration and is more effective in restoring normal liver function and morphology than is the older carbohydrate regime (66, 117, 177, 179, 182).

Another interesting manifestation of hypoproteinism is the fact that the patients do not tolerate parenterally given saline solutions very well. Peripheral and pulmonary edema are often precipitated by what for the healthy individual would be only a moderate dose of salt (1, 16, 48, 49, 80). This is true especially in the postoperative state. In certain of these cases potassium deficiency may

TABLE I.—CAUSES OF HYPOPROTEINISM

I. Lack of protein metabolites
  A. Inadequate diet
    1. Anorexia
    2. Senility
    3. Dietary restrictions (peptic ulcer)
    4. Esophageal, pyloric obstruction.
  B. Poor absorption
    1. Regional enteritis and ulcerative colitis
    2. Enteric fistulas
    3. Carcinoma of stomach (17)
    4. Postoperative total pancreatectomy (95, 175)
    5. Cystic fibrosis of pancreas and celiac syndrome
    6. Sprue

II. Excessive loss of protein metabolites
  A. Draining Wounds (51) (See Table III)
    1. Empyema
    2. Chronic osteomyelitis
    3. Decubitus ulcer (168)
    4. Fungating neoplasm
    5. Postoperative drainage (abdominoperineal resection, mastectomy)
  B. Burns (107)
    1. Acute—local edema and bleb formation
    2. Chronic—weeping, granulating wounds
  C. Internal losses
    1. Acute peritonitis, pancreatitis
    2. Acute intestinal obstruction (81)
  D. Renal diseases with albuminuria (157)
    1. Nephrosis
    2. Chronic glomerulonephritis
    3. Amyloidosis
  E. Increased protein breakdown for gluconeogenesis in thyrotoxicosis, pyrexia, uncontrolled diabetes, and Cushing's syndrome (208)

III. Increased protein need
  A. Pregnancy, lactation

IV. Metabolic dysfunction
  A. Liver disease (123)
    1. Cirrhosis
    2. Chronic hepatitis
    3. Hepatorenal syndrome
  B. Carcinoma of gastrointestinal tract (4, 15)

also play a part (114, 139). Further discussion of electrolyte disorders is beyond the scope of this article, but Coller's warnings (48) regarding salt intolerance are well supported by clinical experience (139).

In patients with carcinoma of the gastrointestinal tract, hypoproteinism is often severe as well as resistant to therapy (16). It has been suggested that in addition to delayed absorption (17) there is some metabolic dysfunction in these patients which prevents normal synthesis of serum protein (4, 15). This is apparently true even in the absence of liver metastases. It has been stated that after surgical extirpation of the malignancy, hypoproteinemia (232) tends to persist for some weeks even though during this period a significant degree of tissue protein repletion occurs (113). Although the nature of this abnormality has yet to be delineated, it is clear that patients with gastric carcinoma require unusually intensive protein therapy prior to operation (176).

METABOLIC EFFECTS OF INJURY OR OPERATION

Profound metabolic alterations are initiated by the stimulus of a major operation. Considerable breakdown of endogenous protein occurs during the early postoperative period (29, 58), so that a patient undergoing a major operation may lose 250 grams of protein (over 1,200 gm. of muscle tissue) during the first 5 postoperative days (225). A sharp drop in the albumin, the lipid, and the alpha amino acid concentrations of the serum occurs following operation, injury, or acute infectious disease (151, 174). Liver function is temporarily impaired following operation as shown by the bromsulfalein, hippuric acid, and urobilinogen excretion tests (120, 212). Renal function, likewise, is briefly impaired following surgery (50), which results in a transient oliguria. There is a slight increase in plasma and interstitial fluid volume which may persist for 10 days following operation (144).

All of the described manifestations occur in normal healthy persons in response to operation. The severity of these metabolic changes varies in a general way with the magnitude of the operation (120, 174), and the changes occur with both spinal and inhalation anesthesia. Protein breakdown is sharply increased by nausea, vomiting, fever (9, 31), wound infection, or atelectasis (120), as well as by acute infectious diseases (98). It is interesting to note that enforced bed rest in normal people results temporarily in negative nitrogen balance (63,228), and that early ambulation seems to inhibit postoperative protein catabolism to a slight extent (120). If the patient is in a chronic state of protein depletion before submitting to the acute trauma of operation, the picture is greatly altered. The protein breakdown is markedly inhibited (31, 32) and protein seems to be utilized more efficiently in these patients even in the early postoperative period. In these cases the serum albumin, lipid, and amino acid concentrations, often already low, are only slightly altered following surgery (151).

Many theories have been advanced to explain these posttraumatic phenomena. Cuthbertson (58) has presented evidence of an increased rate of tissue protein breakdown, while Peters (174) postulates a period of "antianabolism" wherein protein synthesis in the body is inhibited. Albright (6) incriminates the "S" hormone of the adrenal cortex as the agent responsible for the

antianabolic period. This has been related to the general "alarm reaction" of Selye. Werner (227) suggests that the sharp reduction in caloric intake, which usually accompanies operation and injury, may be the entire explanation of the posttraumatic period of protein catabolism.

There are practical applications which can be derived from these extensive postoperative metabolic studies: first, it is of great importance to remember that protein depletion may be treated with far greater efficiency prior to operation than following operation. Recent progress in the field of parenteral protein therapy has made it possible to administer proteins immediately after surgery, but this must never be thought to compensate for inadequate preoperative nutritional repletion. Second, during the postoperative period the patient in a good state of nutrition need not receive any special regimen of protein therapy, as it is almost impossible to achieve a positive nitrogen balance in such a case for the first 3 to 5 days (60), and by that time a full diet is usually well tolerated. The routine postoperative parenteral use of protein hydrolysate (71, 72, 73) in the well nourished patient has no basis in scientific fact and has never been shown to contribute to a smoother convalescence. In the case of the depleted patient there is reason to believe that protein therapy is effective early in the postoperative course (32, 55, 174, 225). Third, therapeutic agents which in a specific patient produce repeated side reactions such as nausea, vomiting, or diarrhea should be avoided as these side reactions themselves may result in considerable protein breakdown.

OPTIMAL PROTEIN DOSAGE IN REPLETION THERAPY

While the National Research Council has recommended a protein intake of 1 gram per kilogram of body weight per day as a maintenance dose for normal men (84), this amount of protein is inadequate for the rapid repletion of wasted tissues. Considerable emphasis has been placed on the mere achievement of nitrogen balance in debilitated patients. This is not enough. Animals kept precisely in nitrogen balance, frequently show low liver protein, plasma protein, and hemoglobin concentrations (220). Far more desirable is a highly positive balance, consistent with the fabrication of the largest possible quantity of new tissue. Allowance must be made for the endogenous "wear-and-tear" protein breakdown, for protein lost by draining wounds, fistulas, and empyema cavities, and for the increased catabolism which occurs in hyperthyroidism. In addition, a large excess must be provided to rebuild the previously lost tissue protein. It is impossible to predict with accuracy the protein requirement for nitrogen balance in any individual patient (109). Therefore, one should aim at administering the maximum dose which can be utilized rather than attempt to estimate the minimum dose necessary for nitrogen balance.

TABLE II.—MANIFESTATIONS OF HYPOPROTEINISM

1. Lowered resistance to blood loss; increased susceptibility to shock (69, 180)
2. Lowered antibody production (24, 37); lowered resistance to infection (40, 99, 150)
3. Impairment of wound healing (138, 215); more frequent postoperative wound dehiscence (125, 126, 137, 215)
4. Bone atrophy (18) and impaired healing of fractures (184)
5. Liver dysfunction and fatty infiltration (13, 76, 93, 100, 105, 106, 136, 169); increased susceptibility to liver poisons (chloroform, arsphenamine) (94, 161, 177)
6. Anemia (156, 170, 171, 224); impaired hemoglobin regeneration after venesection (134)
7. Diminished tissue proteins (5, 137)
8. Hypoalbuminemia (223)
9. Diminished plasma volume (variable) (157)
10. Increased volume of interstitial fluid compartment (54, 104, 112)
    - Generalized tissue edema (119)
    - Edema at site of gastrointestinal anastomosis with obstruction (20, 181)
    - Delayed gastric emptying time (154)
    - Salt intolerance (1, 16, 48, 49, 80)
11. Weight loss.
12. Weakness, lassitude, mental depression, pallor, low pulse rate, blood pressure, and basal metabolic rate (236)

In general, the depleted organism utilizes protein in direct proportion to the dose administered. Human nitrogen balance experiments have shown excellent protein retention (from 40 to 120 grams per day) with oral dosages of from 3 to 6 grams of protein per kilogram per day (55, 129). Hydrolysates and special protein concentrates were used in these cases because it is almost impossible to administer such huge doses (from 200 to 420 grams) daily in the form of whole food protein. Co Tui (53) has demonstrated that the rate of weight gain in these patients also varies directly with the dose of nitrogen administered.

In view of recent criticism of using the nitrogen balance as a means of assaying the worth of protein therapy (165), it is interesting to note that Benditt and his coworkers (23), using a different method, found the same result in depleted rats. These workers chemically analyzed the rat carcass for protein on various repletion dosages of whole protein. Their finding that at constant caloric intake, increasing the dietary protein resulted in

TABLE III.—DAILY PROTEIN LOSS IN EXUDATIVE CONDITIONS

Diagnosis	Date of injury or operation	Date of collection	Total N exuded in 24 hr. gm.	Equivalent in proteins gm.	Equivalent in plasma c.c.
Avulsion of perineum and back	7/7	10/23	6.37	39.81	664
Radical mastectomy	10/25	10/26	4.26	26.65	445
		10/30	1.2	7.50	125
Abdominoperineal resection (infected)	8/9	8/18	6.97	42.46	707
		8/21	3.47	21.69	361
Lung abscess Pyothorax	—	4/24	9.57	59.8	996
Empyema	—	—	9.37	58.56	976

(From Co Tui, *J. Am. Diet. Ass.*, 1946, 22: 97)

a proportionate increase in the rate of tissue protein fabrication, as illustrated in Figure 1.

The subject of protein dosage was admirably summarized by Benditt *et al.* (25) as follows: "Man can easily use up to four grams per kilo per day of protein. We cannot overemphasize the fact that there is a fundamental difference between the maintenance of the equilibrium state in the fully grown and healthy adult and the construction of new tissue in the depleted individual. In order to obtain good rates of tissue synthesis under these latter conditions, it is necessary to feed at protein intake levels of the order of 2–4 gm./kilo./day. The higher protein intake levels have two advantages: first, a greater absolute rate of protein storage, and second, a higher gross efficiency of protein utilization."

PARENTERAL PROTEIN HYDROLYSATES

The subject of parenteral administration of protein hydrolysates has been capably reviewed by Elman (70, 71, 73) and only the fundamentals will be summarized here. Parenterally administered amino acids seem to be metabolized in the liver in a manner similar to the metabolism of amino acids reaching the liver by the portal vein following the digestion and absorption of natural food protein. During the process of protein hydrolysis, hydrogen and hydroxyl groups are incorporated into the molecule. For this reason, 100 grams of the hydrolyzed products are equivalent in nitrogen content to only about 75 grams of whole protein.

As much as 11 per cent of the injected amino acids and peptides are excreted unchanged in the urine (73), but whereas less than 5 per cent of the amino acids of a protein hydrolysate is lost in the urine, from 36 to 53 per cent of the injected peptide fraction is wasted (46, 64). Despite this fact, partial hydrolysates containing large peptide fractions were found to be just as effective parenterally in maintaining nitrogen balance as complete hydrolysates of low peptide content (187). This is in line with the evidence of other workers (234), that there is an unidentified growth substance in the peptide fraction which improves nitrogen retention. The substance is probably identical with "strepogenin," described by Wooley. It is destroyed by complete acid hydrolysis. This may explain why mixtures of crystalline amino acids are not as effective in maintaining body weight in dogs as is whole protein (159, 188).

It has been demonstrated that protein hydrolysates can be effective in the maintenance of nitrogen balance in man (Table IV) and animals, as well as in the regeneration of depleted serum proteins (71, 147). If protein synthesis is to occur, all the essential amino acids (193) together with the energy supply must be available simultaneously (39, 192). In animal experiments, if but one of the essential amino acids was withheld for a period of from 2 to 6 hours, a large portion of the amino acids was wasted (38, 86, 87).

Reactions to properly prepared hydrolysates are uncommon. Elman (72) noted an incidence of less than 1 per cent in giving 2,729 liters of amigen. Others (61, 101) have reported incidences of 3 and 4 per cent. The nature of the reactions has usually been chills, fever, nausea, and vomiting. Nausea has been thought to be due to the glutamic acid content of the infusion (204), and is usually minimized by slowing down the rate of administration.

The various commercial protein hydrolysates differ from one another with regard to the raw material used (casein, blood fibrin, fish protein) and the method of hydrolysis (acid or enzymatic). The more commonly used products are amigen, an enzymatic hydrolysate of casein; parenamine, an acid casein hydrolysate; aminosol, a partial acid hydrolysate of fibrin; and travamin, an enzymatic hydrolysate of bovine plasma. At this time there is insufficient comparative data to decide conclusively about the relative merits of these various hydrolysates. Amigen and parenamine have been shown to be capable of maintaining nitrogen balance in human beings (Table IV). Mixtures of the essential crystalline amino acids have been used with success in man (225). This agent rarely produces nausea or vomiting, but is not yet available for clinical use. The experimental use of ossein gelatin in combination with hydrolysates has been reported (186).

Contraindications to the parenteral administration of hydrolysates are limited to renal in-

sufficiency with uremia and acute congestive heart failure. The question whether severe liver insufficiency also constitutes a contraindication depends on the degree of impairment of the liver function. In most cases of liver disease protein supplements are well utilized (135), but when hepatic insufficiency is advanced to the point where there is failure of the deamination mechanism, amino acid therapy is probably harmful. In such patients the state of hepatorenal failure is usually irreversible with any form of therapy. The positive indications for the use of hydrolysates by the parenteral route are to be discussed.

OPTIMAL DOSAGE OF GLUCOSE AND AMINO ACIDS FOR PARENTERAL REPLETION THERAPY

When a patient can ingest a regular diet, adequate in whole protein foods, his caloric requirement is usually satisfied automatically. However, when purified protein concentrates and derivatives are utilized, consideration must be given to the balance between protein and calories in order to achieve the optimal "protein-sparing" effect. This is especially important in parenteral therapy when complete caloric replacement cannot be achieved without the use of markedly hypertonic solutions or huge volumes of intravenous fluid. When fat emulsions for intravenous use become available, this source of difficulty will be removed, and it will be possible to supply complete caloric as well as protein needs with intravenous therapy (34, 103). This has already been experimentally demonstrated in dogs (152, 155), and in man (202). However, at this time it is still important to know what proportion of intravenous protein hydrolysate is utilized to replace tissue protein and what proportion undergoes gluconeogenesis and combustion to help fulfill the energy requirement.

Commenting upon this problem, Elman (71, 75) has stated that the administration of 100 grams of glucose a day is probably sufficient to prevent endogenous protein breakdown, provided enough exogenous protein is provided. He postulates that the body's fat deposits will supply the remainder of the energy requirement. The work of Gamble (85) is quoted by Elman to support the contention that 100 grams of glucose provides a maximum protein-sparing effect, and that therefore a greater dose need not be included in the daily parenteral ration. Gamble and his coworkers found that *during absolute fast*, there was a daily endogenous protein loss of 80 grams. This loss could be reduced to 40 grams if 100 grams of glucose were given daily. Under these conditions, i.e., complete protein privation, increasing the glucose further did not greatly reduce the negative nitrogen balance. Then, in the attempt to eliminate this protein breakdown, 40 grams of protein as well as the 100 grams of glucose were given. "Only a small further protection of body protein was obtained. Evidently, under the circumstance of sub-energy maintenance intake, ingested protein is oxidized in support of the energy metabolism. . . ." (85). Therefore, despite the intake of 100 grams of glucose and despite the presence of body fat stores, considerable protein breakdown persisted on a 40 gram protein allowance. When Schwimmer and McGavack increased the caloric intake to 900 calories by giving more glucose or fat per os, not only was protein catabolism inhibited, but a positive nitrogen balance was attained on the same protein intake of 40 grams a day. In other words, only in complete protein starvation did 100 grams of glucose constitute a maximal protein-sparing dose. Johnson and his associates (118) failed to confirm even this fact. They reported that adult human males on a protein-free diet lost less nitrogen on a 2,000 calorie than on a 1,200 or 600 calorie intake. If nitrogen retention is desired, it is certain that more calories

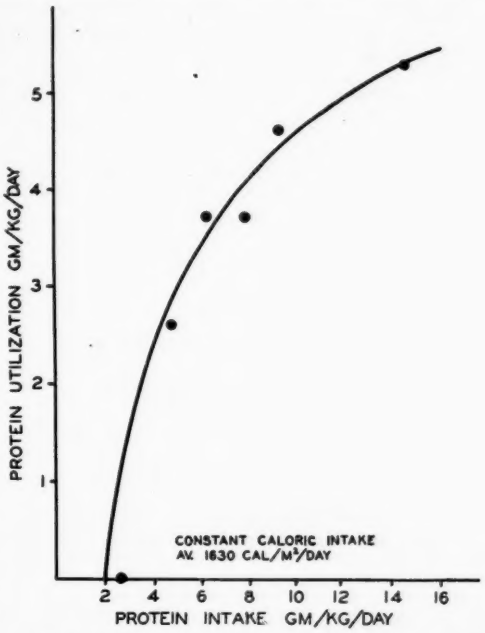


Fig. 1. Effect of increasing protein intake on the degree of protein utilization, i.e., new tissue fabrication. (From E. P. Benditt *et al. J. Laborat. Clin. M.*, 1948, 33: 257.)

TABLE IV.—NITROGEN BALANCE STUDIES OF DEPLETED PATIENTS WITH VARYING PROTEIN AND GLUCOSE INTAKES

Author	Therapeutic agent	Dosage gm. per 24 hr.	Calories per 24 hr.	Glucose gm. per 24 hr.	Nitrogen balance 24 hr.	Remarks
Elman (68)	Amigen (intravenous)	50	1380	300	−0.2	
		60	1420	300	0 to −1	
		60	1420	300	0 to −1	
		60	1420	300	+2 to +3.5	
Mok (162)	Amino acids Lyophilized (intravenous)	60	689	.	0	
		60	1192	*	+0.8	Same patient
		60	3195		+0.6	
		80	1743	*	−1.5	Same patient
		80	3264		+0.4	
		80	1756	*	−1.0	Same patient
		80	3270		−0.6	
Bigham (26)	Amigen (intravenous)	75	1670	350	+0.5	
		70	1555	325	−2.0	
		90	1830	375	+0.4	
Kozoll (128)	Cutter's (intravenous)	60	1420	300	+0.4	Same patient
		90	1530	300	+3.4	
	Parenamine (intravenous)	60	1820	400	−0.8	Same patient
		90	1930	400	+2.1	
	Parenamine (intravenous)	60	1420	300	−2.2	Same patient
		120	1620	300	+5.6	
	Cutter's	120	1240	200	+3.3	
	Parenamine	135	1290	200	−2.0	
Ellison (67)	Amigen (intravenous)	100	1166	200	−0.9	Same patient
		150	1750	300	+1.6	
		150	1155	150	+0.9	Same patient
		150	1750	300	+2.8	
		150	2385	450	+4.4	
Brunschwig (33, 35)	Amigen (intravenous)	150	1749	300	+3.9	Average for 12 da.
		150	1749	300	+3.9	Average for 6 da.
Kremen (131)	Amigen (intravenous)	150	1700	290	+6.	
		150	2100	390	+2.5	
		200	1530	200	+6.7	
Hoffman (109)	Amino acids Lyophilized (intravenous)	58	over 2000	*	−0.7	Same patient
		87			+1.1	
		116			+0.6	
		180			+4.0	
		50		*	+1.5	Same patient
		160			+6.1	
		94		*	+1.1	Same patient
		200			+13.2	
		47		*	+1.0	Same patient
		180			+10.1	

TABLE IV.—NITROGEN BALANCE STUDIES OF DEPLETED PATIENTS WITH VARYING PROTEIN AND GLUCOSE INTAKES—Continued

Author	Therapeutic agent	Dosage gm. per 24 hr.	Calories per 24 hr.	Glucose gm. per 24 hr.	Nitrogen balance 24 hr.	Remarks
Albright (8, 9)	Amigen (intravenous)	150	1749	300	−2.6 to −6	Nondebilitated patient
		200	1930	300	0	Preop. \ Same patient; Postop. / Nondebilitated
		200	1930	300	−5. to −9	
Browne (32)	Whole protein per os	100	3000	*	+1.5	Nondebilitated
		100	3000	*	+5.	Debilitated
		156	3300	*	+8.3	Same patient; debilitated
		156	4000		+10.4	
		200	4200		+12.3	
		156	3100	*	+10.	Same patient; debilitated
		94	2900		2.5	
Kozoll (129)	Essenamine (lactalbumin) per os	50 to 90	2200	*	0	Average for 10 of 11 debilitated patients
		200	2700	*	+12.	Average for 12 debilitated patients; actual nitrogen balance varied from +6. to +20.

*These patients received some of their nonprotein calories by mouth in the form of fat. Exact glucose intake is not available.

N.B. One gram of nitrogen is equivalent to 6.25 grams of whole protein. A nitrogen balance of +10. grams points to retention of 6.25×10.00=62.5 grams of protein by the body. This is equivalent to approximately 300. grams of muscle tissue or 1,000 cubic centimeters of plasma.

Calories are calculated by allowing 4. calories per gram of glucose and whole protein, and 3.66 calories per gram of protein hydrolysate (33).

These nitrogen balance studies were not made during the postoperative catabolic period unless otherwise stated.

are necessary for maximum protein-sparing than are provided by 100 grams of glucose.

What daily caloric intake is necessary in order to achieve rapid restoration of protein deficiencies? In an effort to provide a solution to this problem, we have extracted from the literature numerous nitrogen balance studies on nonoperative patients in which caloric data were included. These representative cases are listed in Table IV. Intravenous administration of protein hydrolysate was the only source of nitrogen unless otherwise stated.

At low levels of amino acid intake (60 to 80 grams) even large caloric intakes (2,000 to 3,000 calories) do not consistently result in a positive nitrogen balance. In fact, Hoffman *et al.* (109) found that some patients on a 2,000 calorie intake were not in equilibrium until they were given almost 3 grams per kilogram of protein hydrolysate. These patients may not have been as badly depleted as some of the others, for depleted patients are believed to utilize their protein more economically than well nourished persons (31, 174). The efficiency of protein utilization increases as larger doses are given (25, 71, 199). Kremen, for instance, noted that when 50 grams of amigen were given, the daily urinary nitrogen output increased, so that almost all the amino acids administered could be accounted for in the urinary nitrogenous wastes. If 150 grams were given with 300 grams of glucose, excellent positive balances were attained.

In general, it can be seen from Table IV that there is no consistently important degree of nitrogen retention with dosage levels below 150 grams of protein hydrolysate and 300 grams of glucose. This would provide 1,750 calories, approximating the basal fasting requirement of the average-sized adult at bed rest (19). Actually, that part of the protein hydrolysate which is retained as newly synthesized tissue protein is not catabolized and has no caloric value to the body. Thus, the body fat stores must be supplying some part of the energy requirement in these patients, but the evidence indicates that the proportion of the total requirement which the body fat can supply is limited. Keeton (121) noted that obese patients seemed to maintain nitrogen balance on a somewhat lower caloric intake than was required by normal individuals.

If the dosage which has been recommended is adopted, it will be necessary to use at least 3,000 cubic centimeters of a 5 per cent solution of protein hydrolysate in 10 to 15 per cent glucose. This requires from 6 to 12 hours to run in. At these rates there is no appreciable glycosuric or diuretic effect from the hypertonic glucose solution (42, 67). Others (143, 67) have used equally hypertonic solutions with satisfactory results. It is probably not worth while to give protein hydro-

lysates in smaller doses than this to patients who cannot take any food by mouth, as there is a good chance that there will be little, if any, nitrogen retention. We cannot agree with Elman (71) that "the malnourished patient unable to eat at all" will profit greatly from 2 liters of 5 per cent amigen in 5 per cent glucose daily, even if supplemented, as recommended, by a third liter of glucose in saline solution.

Some workers (11, 131, 158) have included the nitrogen of plasma and whole blood in their daily balance sheets. This is a confusing practice. Blood protein and hemoglobin are metabolized slowly and perhaps through channels entirely different from oral proteins and parenterally given hydrolysates (149). If the nitrogen balance method is to be applied to these agents, the balance sheet must be continued for a week or more after the plasma has been given (7, 71, 222); otherwise, misleadingly great degrees of nitrogen retention will be noted.

There are practical disadvantages in the use of a parenteral procedure which necessitates a long, tedious period of immobilization for the patient. This is one reason why intravenous protein hydrolysates should not be depended upon as the chief form of therapy in any patient who is able to take food or liquid concentrates by mouth. In these cases, Benditt (25) recommends at least 2,600 calories per day orally of nonprotein foodstuffs. On the other hand, if the intravenous route must be used as the primary therapeutic agent, the protein and carbohydrate dosage should be made large enough to insure that significant tissue protein synthesis will take place.

COMPLETE INTRAVENOUS ALIMENTATION; THE FEEDING JEJUNOSTOMY

A decade ago surgeons, faced with the problem of preparing a severely depleted patient with complete esophageal or pyloric obstruction, had no choice but to construct a feeding jejunostomy. This procedure has been recommended for obstruction due to stomal edema following subtotal gastrectomy (10). The jejunostomy carries with it many problems, not the least of which is the frequent complication of diarrhea. Many different types of aliment have been suggested to counteract this diarrhea (41, 110, 111, 185, 209), but none has yet proved completely satisfactory. Of course, considerable amounts of nitrogen are wasted in the diarrheal discharge (185). Hollander (111), with a formula based upon protein hydrolysate, and Case *et al.* using a homogenized milk and hydrolysate mixture, have reported low incidences of diarrhea.

Today patients can be kept in positive nitrogen, if not caloric, balance by means of parenteral therapy exclusively. To what extent can this technique replace the feeding jejunostomy? Actually, most patients with esophageal or pyloric obstruction present themselves to the surgeon while the obstruction is still incomplete. In these patients an intensive oral feeding program of liquid protein concentrates can be remarkably effective (217). When the obstruction is complete, many of the patients can be successfully repleted on a complete intravenous diet of glucose, protein hydrolysate, whole blood, and plasma or albumin. At present, some of these patients, especially those with poor superficial veins and those who require unusually prolonged repletion therapy, may still require a jejunostomy.

There is a group of cases in which there may exist a positive indication for the complete intravenous diet. This stems from the fact that complete oral starvation reduces the gastrointestinal secretions and motility, which places the gut at rest (26, 173). This is invaluable in colitis due to mercuric chloride poisoning (174). Also, in cases of external fistulas involving the small bowel considerable diminution in the fistulous drainage has been noted by several observers (26, 74). In 1 case, complete parenteral feedings for a period of 2 weeks contributed to the spontaneous closure of a large postoperative ileocutaneous fistula (42). When there is a high external fistula (duodenal, jejunal), the volume of drainage may reach from 3,000 to 4,000 cubic centimeters a day. In such cases "splinting the gastrointestinal tract" by enforced starvation is less likely to result in the drying up of this fistula than of an ileocutaneous fistula. In these high fistulas, jejunal feeding, which by-passes the fistula, is usually preferable (21). This may be accomplished by (1) inserting a Cantor or Miller-Abbott tube for feeding purposes beyond the site of the fistula, (2) passing a catheter through the fistulous tract into the distal loop of small bowel, or (3) making an operative jejunostomy. Meticulous attention must also be paid to the electrolyte balance in these cases. In many cases of gastrocolic fistula, the parenteral route alone can replete the patient sufficiently so that a definitive repair may be successfully completed in one stage.

In patients with severe regional enteritis or ulcerative colitis, attempts to replace protein losses by oral feedings often aggravate the diarrhea and bleeding to a dangerous degree. In many of these patients oral starvation combined with intensive parenteral therapy during the preoperative period may actually result in a temporary

remission of the disease (146, 148, 172, 183). At operation, following a period of exclusively parenteral feeding, the bowel is usually found deflated and clean (26, 74). This is especially valuable in patients requiring resection for multiple intestinal fistulas. Patients with acute intestinal obstruction of the mechanical type, while undergoing long tube decompression, are likewise benefited by intravenous alimentation until oral feeding may be re-started. It has been emphasized (173, 174) that in order to achieve maximal splinting of the gastrointestinal tract, probably not even sips of water should be allowed per os.

Howard (26, 115) and others (8) have recommended the addition each day of 3.0 grams of potassium chloride to the intravenous mixture in cases in which nothing is given by mouth. Except in patients with renal damage, this is a physiologically sound procedure (114, 139) which deserves extensive clinical trial. Vitamin B complex and large doses of ascorbic acid should be either added to the infusion daily with aseptic precautions or given intramuscularly. Our method has been to give 3,000 cubic centimeters or more of 5 per cent amigen in 10 or 15 per cent dextrose divided into two doses to allow the patient a period of ambulation between infusions. From 2 to 3 hours are allowed for each liter unless nausea results. In this case the rate must be decreased to fit the peculiarities of the individual. Unfortunately, the commercially available hydrolysates come in 5 per cent dextrose solution. In practice 1,500 cubic centimeters of 10 per cent amigen and 1,500 cubic centimeters of 20 per cent dextrose in water are allowed to run into the same vein simultaneously through a single needle. This is the equivalent of 3 liters of 5 per cent amigen and 10 per cent dextrose. The limiting factor of this technique is the occurrence of a superficial chemical phlebitis at the sites of injection as a result of the hypertonicity of the solution. If small calibered needles are used and if the sites of the infusion are carefully selected and changed daily, the same veins of the forearm may be repeatedly utilized by a person skillful at venipunctures. In some cases, it is helpful to pass a polythene catheter into a superficial vein for the repeated administration of infusions over a period of days.

This program is supplemented by repeated 500 cubic centimeter blood transfusions until the blood count is normal. Plasma or albumin supplements should also be used daily (131) if the parenteral diet must be continued for more than a week. Satisfactory clinical results have been obtained in patients who have depended upon intravenous nutrients exclusively for periods ranging from 2 to 8 weeks (8, 9, 33, 35). Butler and Talbot warn against the prolonged use of parenteral therapy because the exact requirement of the body for the less well known intracellular electrolytes (potassium, magnesium, calcium, phosphate) has as yet not been determined. Nevertheless, in the face of an enteric fistula or severe ulcerative enterocolitis a 2 or 3 week trial of parenteral therapy may be indicated. During this period, clinical and chemical evidence of calcium and potassium deficiencies should be sought so that these may be corrected.

In patients with severe acute electrolyte derangement (e.g., small intestinal fistula, high intestinal obstruction) there is frequently a prerenal azotemia. It is probably wise to correct the electrolyte disorder and azotemia before considering intravenous alimentation with large doses of protein hydrolysate. Amigen contains from 2.0 to 2.5 grams of sodium chloride per liter (71). If maintenance therapy calls for greater amounts of salt, as in the case of high fistulas, hypertonic saline solution may be added to the intravenous mixture.

THE ORAL VERSUS THE PARENTERAL ROUTE OF PROTEIN THERAPY

In one respect it is unfortunate that the parenteral route of protein therapy has received so much attention in recent years, because it has served to give many surgeons a false sense of security. One or two liters of protein hydrolysate are frequently ordered for the patient, and then little attention is paid to the oral intake. Peters (174) has emphasized that this is a short-sighted procedure as the hydrolysate infusion immobilizes the patient for prolonged periods and often produces nausea with the net result that his oral intake is reduced by a greater amount than is taken intravenously. The oral route should receive primary attention in all patients except those with complete intestinal obstruction, peritonitis, ileus, high enterocutaneous or gastrocolic fistula, regional enteritis, and ulcerative colitis.

Aside from the teleological reasoning that the natural route is usually the best, there is abundant evidence (14, 109, 130, 147, 148, 203) to show that patients receiving the same dose of protein hydrolysate intravenously and by mouth show better utilization by the natural route. Also, if the oral route is utilized, then one is not restricted to the use of hydrolysates. And if high quality whole protein is taken per os, utilization seems to be more efficient than if an equivalent dose of amino acids is ingested (146, 148). Dogs which were fed

adequate amounts of crystalline amino acids by mouth lost weight, whereas equivalent dosages of whole protein maintained the dogs' body weight successfully (159, 188). This phenomenon was noted by Elvehjem in rats but did not occur when Chow (44, 45) compared whole casein with an equivalent quantity of a *partial* casein hydrolysate in rats. Regardless whether or not whole protein is actually superior to various hydrolysates, there can be little question but that any plan of protein therapy must focus its attention on the oral route whenever possible. It is the only practical route by which an excess of calories (from 3,000 to 3,500) as well as proteins can be given.

Ideally, every patient should receive individual study by a skilled dietitian in order to achieve the highest possible protein food intake. However, few hospitals have sufficient dietetic personnel for such close supervision, and few institutional kitchens can produce food that is continually appetizing and attractive to patients having a multitude of different diet habits and prejudices. Furthermore, even with conscientious and individualized dietetic attention, it is unusual to have a depleted patient eat more than from 70 to 90 grams of whole food protein per day. When the patient is without appetite and too weak to cut and chew his food, even this intake is unattainable because of the large bulk of natural food products. Thus, while it is easy for the physician to order a "high protein diet," and while it is possible for the dietitian to put 100 grams of protein on the patient's tray each day, it is all too common for the actual daily intake to be between 40 and 60 grams.

A solution to this problem lies in the use of concentrated protein supplements. Perhaps the most deservedly popular of these is dried skimmed milk powder. This contains 35 per cent whole protein (casein and lactalbumin) of high biological value. The cost is low—about $0.35 per pound, retail, in New York City. A liquid concentrate containing 120 grams of skimmed milk powder, 6 eggs, 2 egg whites, and 300 grams of lactose or cane sugar to 1,000 grams of skimmed milk has been recommended by Varco (218). This gives 120 grams of protein in 1,500 cubic centimeters of liquid, and if no solid food can be taken, 3 liters of this concentrate per day will provide excellent repletion therapy. This preparation, in our experience, has produced two annoying side reactions: nausea and diarrhea. The former often disappears when the patient becomes accustomed to the mixture, and in other cases can be assuaged by reducing the high sugar content. Diarrhea is minimized by observing sterile precautions in preparation. In some cases we have had fewer reactions when the floor nurse was instructed to add between 30 and 40 grams of skimmed milk powder, 1 egg, from 10 to 15 grams of essenamine or protolac, and flavoring to the 8 ounces of skimmed or whole milk after each meal and at bed time. This supplement alone provides the equivalent of 120 grams of protein a day. Several satisfactory but expensive commercial protein preparations are available (see Table V). Baby foods, such as homogenized meats, have a low satiety level and are often a valuable adjunct (54).

Some clinics have emphasized the oral use of protein hydrolysates, contending that this product spares the organism the "burden" of digesting the protein (52). Actually, there is no physiological evidence that predigestion offers any advantage whatever, with a possible exception in patients suffering from regional enteritis and colitis (59, 174). The hydrolyzed products possess the advantage of providing large amounts of protein material in small bulk so that intakes at protein levels of from 250 to 300 grams are possible (55). However, one can frequently achieve equally great intakes by utilizing skimmed milk powder or lactalbumin (see Table V) and thereby avoid the objectionable taste of the hydrolysates. As mentioned, the hydrolysates are efficiently utilized by mouth, even more so than similar products given intravenously. Encouraging results in the treatment of ulcerative colitis with oral hydrolysates were reported by Machella, contrary to the findings of earlier workers (146).

In short, the problem of insuring adequate oral protein intake consists first in providing as appetizing a high protein diet as possible. This should then be supplemented with the combination of protein concentrates which is best tolerated by the individual patient. Those patients who cannot or will not take even liquid concentrates by mouth should receive forced feedings by nasogastric tube. Recipes for oral and tube feedings are given by Stare and Thorn (208), Lund (142), Lund and Levenson (143), Kozoll and his associates (129), and Varco (217). If side reactions like vomiting, flatulence, or diarrhea supervene, they may conceivably result in the breakdown of more protein than the dietary supplement provides, and thereby necessitate a modification of the repletion technique. Diarrhea should be vigorously combated with opiates, kaopectate and amphogel. Ingenious improvisation is essential if each patient is to receive the highest possible intake with the least possible psychic and organic damage.

TABLE V.—COMPARISON OF PROPRIETARY PROTEIN PREPARATIONS IN COMMON USE

PRODUCT	Prot. content (% of gross wgt.)	CONTENT	Retail price per lb.	Calculated cost per 100 gm. protein
Beefsteak	20		$.90	$.99
Homogenized Baby Meat	20		.80	.88
Starlac	35	Skimmed milk powder	.35	.22
Protolac	65	Milk protein plus hydrolyzed yeast and liver	2.50*	.85
Gerilac	33	Milk protein plus carb., vit., min.	1.19*	.80
Protenum	42	Casein, dextrose, flavor	1.89*	.99
Casec	88	Calcium caseinate	4.00	1.00
Meritene	32	Milk protein, carb., vit., min.	1.63	1.12
Protinal	61	Milk protein, carb.	3.25	1.17
Delcos	50	Milk protein, carb., flavor	3.15*	1.39
Somagen	70	Milk, yeast and liver proteins, carb., vit.	4.59*	1.45
Essenamine	81	Lactalbumin	5.71	1.93
Protolysate	75	Casein hydrolysate	3.49*	1.03
Hydrolysate (Squibb)	84	Casein hydrolysate	4.27*	1.02
Hydrolysate (MRT)	70	Yeast hydrolysate	5.25	1.65
Nutramigen	15	Protolysate, Dextrimaltose, fat, min.	1.39*	2.04
Proral	55	Yeast hydrolysate, lactalbumin, carb., vit., min.	5.30	2.12
Caminoids	45	Beef, grain, yeast and milk protein hydrolysate, carb.	4.73	2.32
Ledinac	50	Liver hydrolysate, maltose, vit.	5.26*	2.32
Hydrolysate (Walker)	60	Casein hydrolysate, vit., min.	6.30*	2.32
P.H.V.	44	Yeast and meat hydrolysate, carb., vit.	6.27*	3.14

*Denotes fair trade minimum price.
carb.=carbohydrates
vit.=vitamins
min.=minerals

THE PLACE OF WHOLE BLOOD TRANSFUSION IN REPLETION THERAPY

In the dynamic protein equilibrium of body proteins, hemoglobin occupies a unique position. Dogs, experimentally depleted of both hemoglobin and plasma protein, raid their own tissue proteins in the attempt to repair these deficits (159, 231). Hemoglobin seems to enjoy a preferential priority call on the available protein in such a situation, as anemic depleted dogs fabricate from two to four times as much hemoglobin as plasma protein (188, 189, 190). To prevent raiding of already depleted tissue protein and to insure optimal utilization of dietary protein for tissue synthesis, it is essential in preoperative patients to correct promptly any hemoglobin deficiency by means of whole blood transfusions (131). This is of benefit in increasing the patient's resistance to operative blood loss. Also, it is a universal empirical observation that the quantitative replacement of hemoglobin deficiencies constitutes one of the most important factors in enabling the patient to withstand successfully such massive operations as pancreaticoduodenectomy, portocaval shunt, and radical pelvic evisceration (229).

TABLE VI.—MEASURED BLOOD LOSS DURING OPERATION

	Range, c.c.	Average loss, c.c.
Thyroidectomy	234–688	373
Mastectomy	529–1091	808
Abdominoperineal resection	183–686	410
Biliary tract, secondary procedures	158–1455	594
Gastric operations, complicated	321–804	599
(from Crook, Iob, and Coller, *Surg. Gyn., Obst.*, 1946, 82: 417)		
Abdominoperineal resection	415–2420	1080
Suprapubic prostatectomy	265–1235	551
Nephrectomy	285–845	478
Lobectomy	1900–3050	2323
Pneumonectomy	1710–2600	2188
Esophagectomy	— —	2375

(from Lenahan, Spitz, and Metcalf. *Arch. Surg.*, 1948, 57: 435)

The use of serial hemoglobin determinations, made by a standard photoelectric method, has been found to be an adequate guide for deciding the quantity of blood to be transfused. From 500 to 1,000 cubic centimeters of whole blood are given daily until the hemoglobin concentration is within normal limits. In a patient of average size (from 65 to 70 kgm.) a transfusion of 500 cubic centimeters will usually result in a hemoglobin rise of more than 1 gram per cent. During the operation there should be a complete replacement of operative blood loss. This loss is usually greater than suspected by the operator. The figures (see Table VI) for average blood loss in carefully performed operations are actually minimum figures as they do not include the not inconsiderable factor of postoperative blood loss (206). Wangensteen and others (132) have advocated actually measuring the weight of the blood lost. If only dry sponges are used throughout the operation, the circulating nurse may then weigh the

sponges before and after use and the difference may be presumed to represent the external blood loss.

While adequate blood transfusion is vital to surgical success, it should not be considered that this therapy will of itself remedy a protein deficit. A 500 cubic centimeter blood transfusion contains in addition to erythrocytes only about 15 grams of plasma protein. The nitrogen within the red blood cell is not readily available to the body protein pool. When fresh blood has been transfused, 8 weeks must pass before half of the transfused red blood cells are found to have become disintegrated (83, 163, 164). Likewise, in polycythemia due to excessive transfusions the rate of disintegration of the transfused erythrocytes is the same as that of the recipient's own red cells, i.e., 0.8 per cent per day (27). Adequate protein dosage, therefore, cannot be approached by means of blood transfusions even if one were willing to accept the risk of hemoconcentration and polycythemia. In preoperative therapy, blood transfusion is utilized chiefly as a rapid and efficient means of replacing the hemoglobin deficiency. The iron released by the disintegration of red cells is re-utilized in the synthesis of new erythrocytes with remarkable rapidity and efficiency (89, 91). In severe anemias in which immediate hemoglobin repletion is necessary, concentrated erythrocyte suspensions may be used (214). It is interesting to note that Strumia has separated the protein fraction from hemoglobin and has used this globin intravenously for protein repletion with successful results. Conversely, normal hemoglobin production in man (134) and animals (188, 230) depends upon the availability of protein raw materials as well as of iron.

Several authors (1, 47) have recently stressed the fact that preoperative patients frequently show a diminution of total blood volume. This is said to be frequently more severe than would be suspected from a simple determination of hemoglobin concentration, which may be deceptively high because of dehydration. Lyons (47) has introduced the term "chronic shock" to describe the syndrome of a decrease in blood volume, proteins, and body weight with a simultaneous increase in interstitial fluid. His group believes that the blood volume should be determined and the hemoglobin deficit calculated "on the basis of standard for usual weight prior to illness." Estimated preoperative transfusion dosages as large as 2,000 cubic centimeters were frequently encountered.

While there can be no quarrel with the principle that deficits in the circulating blood volume must be replaced preoperatively, it is not certain at this time whether it is necessary or desirable that the dosage for transfusion therapy be calculated on the basis of red blood cell volume. Although the dye disappearance curve method (90) is a valuable research tool when meticulously controlled, we agree with Stanton (206) that accurate red cell volume determination is "too difficult technically to be considered practical for routine clinical use." In our hands the 10-minute blood volume test (96) has offered no advantage in calculation of transfusion dosages over *serial* determinations of hemoglobin or hematocrit.

THE PLACE OF HUMAN PLASMA IN REPLETION THERAPY

At first glance, human plasma transfusion would seem to constitute ideal replacement therapy for depletion of the plasma proteins. Actually, transfused plasma, labeled with radioactive isotopes, escapes from the vascular compartment with great rapidity. About 50 per cent of the injected plasma leaves the blood stream within 26 hours to enter the general pool of body protein (82). Over a 7 day period approximately half of the injected plasma undergoes combustion while most of the remainder becomes fabricated into tissue protein (7). Thus, only a fraction of the injected plasma is directly available to rectify the lowered serum protein level (158). Since a liter of plasma contains only 65 grams of protein, huge volumes of plasma are required to replenish depleted tissue as well as plasma protein.

Administered at the rate of about 1,000 cubic centimeters per day over a long period of time, plasma transfusion alone can improve the recipient's serum protein level (11). In fact, Allen, Bogardus, and their associates believe that the use of plasma on this dosage scale is the most efficient means of repleting plasma proteins. Contrary to the findings of Lund (142), they suggest "that the fear of overtransfusion is unwarranted except where the cardiovascular reserve is reduced," since the plasma protein leaves the vascular compartment fairly rapidly. Nevertheless, we do not consider massive plasma transfusion the procedure of choice in protein repletion for several reasons: (1) there is the expense entailed ($1.00 per gram of plasma protein), and (2) the complication of homologous serum jaundice has been found to occur in from 4.3 to 7.5 per cent of all patients receiving pooled human plasma transfusions (30, 198, 205). This is a serious complication, occurring from 60 to 180 days following transfusion, which in some cases has led to fatalities. It is possible that ultraviolet radiation may

eliminate the hepatitis virus from plasma (28, 233), but this procedure has still to be confirmed on a large scale. It is interesting to note that homologous serum jaundice is rarely transmitted by unpooled whole blood transfusion (92, 205) and does not occur following the use of human albumin because the virus does not survive the period of heating during the preparation of the albumin (88).

Some observers (217, 226) believe that injected plasma is metabolized in such a manner that it may not be effective in protecting the liver against fatty infiltration. In this respect whole protein per os or intravenous hydrolysate is believed to be superior to plasma. A final disadvantage of plasma, in cases of hypoproteinemic edema, is the high salt content (5 to 6 grams per liter) which may act temporarily to aggravate the edema.

In cases of shock, when blood is not available, plasma transfusion is indicated in spite of these disadvantages. When there is evidence of extensive loss of serum into wounds (following abdominoperineal resection, pneumonectomy, in empyema, and decubitus ulcer), into the gut (paralytic ileus and acute intestinal obstruction), and into the peritoneal cavity (acute pancreatitis and acute peritonitis), replacement therapy by plasma transfusion constitutes the most direct method of correcting the specific deficit in circulating plasma. Also, in severe burns with hemoconcentration, plasma transfusion is indicated, although evidence has recently accumulated which suggests that early whole blood transfusion may be preferable in many of these cases (2, 79).

In other situations the exact place of plasma therapy is not as yet settled. It is not a physiological means of administering protein in that preformed whole protein enters the vascular compartment without the benefit of prior digestion into amino acids. Although plasma can support nutrition in dogs as the sole source of nitrogen (230), a significant portion of injected plasma does not become incorporated into tissue protein until a period of 5 to 7 days has elapsed (7). Therefore, in elective cases the parenteral use of protein hydrolysate seems more logical than the use of plasma (71). The use of the two agents in combination has been recommended (131), and this recommendation should be followed especially when it becomes necessary to employ the parenteral route exclusively for long periods of time.

THE PLACE OF CONCENTRATED SALT-POOR HUMAN ALBUMIN IN REPLETION THERAPY

In comparison with plasma, human albumin prepared by the Cohn fractionation process (116) does not transmit the hepatitis virus (88) and has a sodium content of only 0.2 gram per 25 grams of albumin, or less than one-tenth that of plasma (197). Its cost to the patient is $2.10 per gram of protein. When it is used in the treatment of protein depletion, human albumin can be given intravenously in limited doses only. Twenty-five grams of human albumin is the osmotic equivalent of 500 cubic centimeters of citrated plasma (196). If as much as 60 grams a day are given over a 10 or 15 day period, heart failure may develop even in patients without previous cardiovascular disease (222). Its metabolic fate is similar to plasma in that about 40 per cent is burned and from 45 to 50 per cent is converted into tissue protein. In 4 to 8 days after completion of the intravenous administration of albumin, about 10 per cent of the albumin remains in the blood stream (222). An intravenous dose of 60 grams of albumin per day seems to produce proteinuria in some patients without evidence of pre-existing renal disease. On the other hand, good results can be obtained with smaller doses (from 25 to 50 grams daily) of salt-poor albumin given intravenously in cases of severe hypoproteinemic edema if it is combined with a proper salt-poor high protein diet over a long period of time (42, 208). Despite the fact that albumin is low in tryptophane and isoleucine (102), Eckhardt and his associates (65) have shown that doses of 37.5 grams given intravenously and 50 grams per os can maintain the human nitrogen balance.

Satisfactory results may be expected with albumin in the treatment of shock. In this situation the concentrated albumin is more effective when diluted to a physiological concentration with saline or glucose solution (56, 140). In other cases of acute protein deficit, in which an emergency operation has forced the omission of preoperative therapy, the use of a pre-formed proteinlike albumin may prove to be advantageous. In cases of postoperative intestinal obstruction due to hypoproteinemic edema at the site of an anastomotic stoma, the judicious use of human albumin may increase the osmotic pressure of the blood and thereby reduce this stomal edema. This may eventually eliminate the necessity for making a feeding jejunostomy in cases of obstruction due to edema following gastric resection. If a patient is properly prepared and a technically sound anastomosis is constructed, this complication is unusual. Elman *et al.* (77) reported satisfactory clinical results with salt-poor human albumin in treating chronic hypoalbuminemia. Whether albumin constitutes a complete substitute for plasma in all the situations in which plasma is indi-

cated, is not yet known. Perhaps the globulin fraction of plasma with its antibodies may prove to be of some specific value to the depleted patients. At present albumin has the advantages of freedom from the hepatitis virus and of low salt content with the disadvantage of increased cost.

A SUGGESTED PROGRAM OF PROTEIN THERAPY

It should be axiomatic that the design for protein therapy must be fitted to the needs and the peculiarities of each individual patient. The occasional patient who reacts to oral administration of protein concentrates with intractable diarrhea should receive supplementary hydrolysate parenterally. The patients who suffer repeated febrile and other side reactions following parenterally administered hydrolysate supplements should be given only oral preparations. Although the use of a certain amount of a protein hydrolysate or a whole protein concentrate daily before and after operation has been advocated as a *routine* measure (62), this type of "shotgun therapeutics" results only in inadequate dosages for the depleted patients, and there is no demonstrable benefit for those in a normal state of nutrition. Actually, the uncomplicated case of cholelithiasis, fibroid uterus, appendicitis, hernia, or hemorrhoids usually requires no protein therapy other than that for correction of possible anemia. When there is only a hemoglobin deficit (menorrhagia), it is necessary to give the patient only whole blood transfusion and iron therapy preoperatively. The exceptions are the patients with evidence of coexisting nutritional deficiency. On the other hand, almost all patients suffering from the conditions listed in Table I should be considered protein-deficient by the very nature of their disease.

A recommended regime for use in clinical practice begins in the out-patient clinic or private office with evaluation of the patient, his disease, dietary history, and recent weight loss. Serum protein and albumin concentrations are determined especially in cases in which the nutritional evaluation is indefinite. A complete blood count should always be made. If the hemoglobin level is below 10 grams per cent, the protein repletion program is better undertaken in the hospital where adequate whole blood transfusions can be administered. Otherwise, in most cases the patient can make an excellent beginning at home by observing a properly planned dietary with supplements of skimmed milk powder, proprietary whole protein, or hydrolyzed protein products. Cooperative patients can ingest from 200 to 250 grams of protein daily at home with proper guidance. Adequate vitamin therapy should be prescribed. During the few weeks preceding a patient's hospitalization for elective surgery—while awaiting bed space or completion of diagnostic study—considerable repletion can be accomplished.

In the hospital the technique of repletion is identical with that practiced at home except that the parenteral route also becomes available. After the patient is in a state of adequate hydration, the blood count and the serum protein and albumin levels may be determined. Whole blood is given in doses of from 500 to 1,000 cubic centimeters daily until the hemoglobin level is within normal limits. As appetizing a diet as possible is given and should include at least 100 or 125 grams of whole food protein. This is supplemented with either Varco's (218) or Lund's (142) formula, or modifications thereof. One ounce of powdered brewer's yeast suspended in iced tomato juice may be given two or three times a day for its protein as well as its excellent crude vitamin B content. If further supplementation seems desirable, 50 grams of protein hydrolysate may be given intravenously after the evening meal. Larger doses usually require that most of the day be devoted to the infusion and often result in a greater loss of oral intake than can be contributed by the parenteral route (174). Plasma and albumin are used on specific indications and are rarely necessary preoperatively unless the parenteral route must be used exclusively or unless hypoproteinemic edema is present. Repletion exclusively by the intravenous route is attempted only on the specific indications previously discussed.

The exact length of time which should be devoted to protein repletion is not known, as there is no good laboratory or clinical test for the adequacy of tissue protein repletion. Varco (217) recommends, on an empirical basis, approximately 5 to 7 days of preparation for each 10 per cent loss of body weight. The patient's weight curve provides a good gauge of the success of nutritional therapy. Occasionally in severely depleted patients a sudden drop in the weight curve occurs after 4 or 5 days of therapy because of profuse diuresis (153). This is probably due to the loss of occult edema (interstitial) fluid and should be followed by a period of slow but steady weight gain.

In the postoperative period the first important factor is the complete replacement of the blood loss due to operation. In the uncomplicated case of gastric or colonic resection the patient is usually taking a fairly adequate soft diet by the third to the fifth postoperative day. This patient often

needs no intravenous administration of fluids after the third day. Since the phase of nitrogen catabolism probably prevents adequate utilization in the early postoperative period, we have not used any special protein preparations in uncomplicated cases with adequate preoperative preparation. The use of Abbott-Rawson orojejunal tube feedings (185) following gastrectomy has not been considered necessary as a routine measure, although in severely depleted patients it is a highly desirable procedure.

Vigorous parenteral protein therapy (3,000 c.c. of 5% amigen in 10% dextrose) is advisable postoperatively only when adequate oral feeding is interdicted because of stomal obstruction, peritonitis, or enterocutaneous fistula. The routine use of parenteral administration of amino acids following gastric surgery has not shown any striking improvement in the patients' clinical courses (225). However, in the presence of various complications (wound infection, intestinal obstruction) protein therapy should certainly be instituted postoperatively. In nonelective cases in which adequate preoperative repletion is impossible, the intelligent parenteral administration of hydrolysates, blood plasma, and albumin in the immediate postoperative period may help prevent the complications which accompany hypoproteinism.

Although it may not seem related to the present discussion, early ambulation is a feature of postoperative management which has an important influence on the metabolic functions of the surgical patient. The early return to activity and vigor improves the appetite and gastrointestinal function, and there is evidence to show that enforced bed rest in itself encourages tissue protein breakdown even in normal people (63, 228). In postoperative patients (120) better nitrogen balances were found after early ambulation than in a control group kept at bed rest. Since it accelerates the return of the gastrointestinal tract to normal function, early ambulation has in our hands been invaluable in simplifying the postoperative management of protein-depleted patients, especially of the older age group.

CONCLUSIONS

1. Protein repletion should be accomplished prior to operation whenever possible. The postoperative parenteral administration of protein hydrolysates should not be considered compensation for inadequate preoperative preparation.

2. Within broad limits, the higher the protein intake (3 to 4 gm. per kilogram), the greater the quantity of new tissue protein produced.

3. The oral route allows more efficient protein utilization than does the parenteral route.

4. Anemia should be promptly corrected by means of whole blood transfusions in order to forestall "raiding" of the tissue protein as a source of the raw materials for hemoglobin fabrication.

5. Sufficient carbohydrate or fat must be supplied to prevent the catabolization of protein for the satisfaction of the energy requirement.

6. Good nitrogen retention in average-sized adults can be achieved by using the intravenous route exclusively only if a minimum of 150 grams of protein hydrolysate and 300 grams of glucose are given each day. The administration of hydrolysates in dosages smaller than this to patients who are unable to take nourishment by mouth is probably not worth while.

7. Successful protein therapy demands individual improvisation so that each patient receives the combination of agents which results in the greatest dosage and the least psychic and physiological disturbance.

SUMMARY

The literature concerning the nature of protein depletion in surgical patients is reviewed. The physiological basis of the various repletion techniques is explored, and the place of whole protein, protein hydrolysate, plasma, albumin, and whole blood in repletion therapy is critically evaluated.

A practical program is offered for the management of protein deficiency.

REFERENCES

1. ABBOTT, W. E., and MELLORS, R. C. Total circulatory plasma proteins in surgical patients with dehydration and malnutrition. Arch. Surg., 1943, 46: 277.
2. ABBOTT, W. E., PILLING, M. A., GRIFFIN, G. E., HIRSCHFELD, J. W., and MEYER, F. L. Metabolic alterations following thermal burns; the use of whole blood and an electrolyte solution in the treatment of burned patients. Ann. Surg., 1945, 122: 678.
3. ABELS, J. C., ARIEL, I. M., PACK, G. T., and RHOADS, C. P. Metabolic studies in patients with cancer of the gastrointestinal tract; lipotropic properties of protein. Proc. Soc. Exp. Biol., N.Y., 1944, 56: 62.
4. ABELS, J. C., ARIEL, I. M., REKERS, P. E., PACK, G. T., and RHOADS, C. P. Metabolic abnormalities in patients with cancer of the gastrointestinal tract. Arch. Surg., 1943, 46: 844.
5. ADDIS, T., POO, L. J., and LEW, W. The quantities of protein lost by various organs and tissues of the body during a fast. J. Biol. Chem., 1936, 115: 111.
6. ALBRIGHT, F. Cushing's Syndrome. Harvey Lect., Balt., 1942–1943, 38: 123.
7. ALBRIGHT, F., FORBES, A. P., and REIFENSTEIN, E. C., JR. Fate of plasma protein administered in-

travenously. Tr. Ass. Am. Physicians, 1946, 59: 221.

8. ALBRIGHT, F., REIFENSTEIN, E. C., JR., and FORBES, A. P. Conference on Metabolic Aspects of Convalescence. Josiah Macy, Jr. Foundation, 1944, 8: 168.
9. Ibid., 1945, 11: 25.
10. ALLEN, A. W., and WELCH, C. E. Jejunostomy for the relief of malfunctioning gastroenterostomy stoma. Surgery, 1941, 9: 163.
11. ALLEN, J. G., BOGARDUS, G., EGNER, W., and PHEMISTER, D. B. Correction of hypoproteinemia by the administration of plasma and blood. Surg. Gyn. Obst., 1948, 86: 604.
12. ALLISON, J. B. Utilization of protein hydrolysates by normal and protein depleted animals. Am. J. Med., 1948, 5: 419.
13. Idem. Metabolism of proteins and amino acids. Annual Rev. Biochem. 1948, 17: 275.
14. ALLISON, J. B., SEELEY, R. D., and FERGUSON, F. P. The determination of nitrogen balance indexes of protein hydrolysates in dogs. J. Biol. Chem., 1947, 171: 91.
15. ARIEL, I. M. The nature of postoperative hypoproteinemia in patients with gastrointestinal cancer. Surg. Gyn. Obst., 1949, 88: 185.
16. ARIEL, I. M., ABELS, J. C., PACK, G. T., and RHOADS, C. P. Metabolic studies in patients with cancer of the gastrointestinal tract; treatment of hypochloremia refractory to administration of sodium chloride, especially in patients with gastrointestinal cancer. J. Am. M. Ass., 1943, 123: 28.
17. ARIEL, I. M., JONES, F., PACK, G. T., and RHOADS, C. P. Metabolic studies in patients with cancer of the gastrointestinal tract; the glycine tolerance test in patients with gastric cancer. Ann. Surg., 1943, 117: 740.
18. ARMSTRONG, W. D., and ESTREMERA, H. Effect of protein deficient diets on the skeleton of the mature rat. Fed. Proc., Balt., 1947, 6: 235.
19. BARD, P. Macleod's Physiology in Modern Medicine, 9th ed., St. Louis: C. V. Mosby Co., 1941.
20. BARDEN, R. P., RAVDIN, I. S., and FRAZIER, W. D. Hypoproteinemia as a factor in retardation of gastric emptying after operations of Billroth I or II types. Am. J. Roentg., 1937, 38: 196.
21. BARTLETT, M. K., and LOWELL, W. H. Acute postoperative duodenal fistula; report of 12 cases. N. England J. M., 1938, 218: 587.
22. BELING, C. A., MORTON, T. V., and BOSCH, D. T. Blood volume and other determinations in preoperative and postoperative care. Surg. Gyn. Obst., 1948, 87: 163.
23. BENDITT, E. P., HUMPHREYS, E. M., WISSLER, R. W., STEFFEE, C. H., FRAZIER, L. E., and CANNON, P. R. The dynamics of protein metabolism; the interrelationship between the protein and caloric intakes and their influence upon the utilization of ingested protein for tissue synthesis by the adult rat. J. Laborat. Clin. M., 1948, 33: 257.
24. BENDITT, E. P., WISSLER, R. W., WOOLRIDGE, R. L., ROWLEY, D. A., and STEFFEE, C. H. Loss of body protein and antibody production by rats on low protein diets. Proc. Soc. Exp. Biol., N.Y. 1949, 70: 240.
25. BENDITT, E. P., WOOLRIDGE, M. A., and STEPTO, R. The dynamics of protein metabolism; the relationship between the level of protein intake and the rate of protein utilization by protein depleted men and rats. J. Laborat. Clin. M., 1948, 33: 269.
26. BIGHAM, R. S., MASON, R. E., and HOWARD, J. E. Total intravenous alimentation, its technique and therapeutic indications. South. M. J. 1947, 40: 238.
27. BIRKHILL, F. R., MALONEY, M. A., and LEVENSON, S. M. Metabolic fate of infused erythrocytes in man. J. Clin. Invest., 1949, 28: 772.
28. BLANCHARD, M. C., STOKES, J., JR., HAMPIL, B., WADE, G. R., and SPIZIZEN, J. Methods of protection against homologous serum hepatitis; inactivation of hepatitis virus SH with ultraviolet rays. J. Am. M. Ass., 1948, 138: 341.
29. BRAASCH, J. W. Protein metabolic response to trauma. Surg. Gyn. Obst., Internat. Abstr. Surg., 1949, 88: 473.
30. BRIGHTMAN, I. J., and KORNS, R. F. Homologous serum jaundice in recipients of pooled plasma. J. Am. M. Ass., 1947, 135: 268.
31. BROWNE, J. S. L., SCHENKER, V., and STEVENSON, J. A. F. Some metabolic aspects of convalescence. J. Clin. Invest., 1944, 23: 932.
32. BROWNE, J. S. L., SCHENKER, V., VENNING, E. H., and JOHNSON, L. G. Conference on the Metabolic Aspects of Convalescence. Josiah Macy, Jr. Foundation, 1946, 14: 170.
33. BRUNSCHWIG, A., BIGELOW, R. R., and NICHOLS, S. Intravenous nutrition for 8 weeks; partial enterectomy; recovery. J. Am. M. Ass., 1945, 129: 441.
34. BRUNSCHWIG, A., CLARK, D. E., and CORBIN, N. Postoperative nitrogen loss and studies on parenteral nitrogen nutrition by means of casein digest. Ann. Surg., 1942, 115: 1091.
35. Idem. Intravenous injection of casein digests in the maintenance of nutrition; a consideration of medicomilitary aspects. Mil. Surgeon, 1943, 92: 413.
36. BUTLER, A. M., and TALBOT, N. B. Parenteral fluid therapy; estimation and provision of daily maintenance requirements. N. England J. M., 1944 231: 585.
37. CANNON, P. R. Proteins in resistance to infection. J. Am. M. Ass., 1945, 128: 360.
38. Idem. Amino acid utilization in the surgical patient. J. Am. M. Ass., 1947, 135: 1043.
39. Idem. Some Pathologic Consequences of Protein and Amino Acid Deficiencies. Springfield: Charles C. Thomas, 1948.
40. CANNON, P. R., WISSLER, R. W., WOOLRIDGE, R. L., and BENDITT, E. P. The relationship of protein deficiency to surgical infection. Ann. Surg., 1944, 120: 514.
41. CASE, C. T., ZOLLINGER, R. N., MCMULLEN, C. H., and BROWN, J. B. Observations in jejunal alimentation. Surgery, 1949, 26: 364.
42. CHASSIN, J. L., and HINTON, J. W. Unpublished data.
43. CHOW, B. F. The electrophoretic studies on the effect of protein depletion on plasma proteins and the regeneration of plasma proteins after oral administration of hydrolysates prepared from casein and lactalbumin. Ann. N. York Acad. Sc., 1946, 47: 297.
44. CHOW, B. F., ALLISON, J. B., and WHITE, J. I. The effect of enzymatic hydrolysis on the nutritive value of casein; digestion of casein with pancreatic enzymes. J. Nutrit., 1948, 36: 231.
45. CHOW, B. F., and DEBIASE, S. Effect of oral administration of casein hydrolysate on total circulating plasma proteins of man. J. Laborat. Clin. M., 1948, 33: 453.

46. Christensen, H. N., Lynch, E. E., and Powers, J. H. The conjugated nonprotein amino acids of plasma; peptidemia and hyperpeptidemia as a result of the intravenous administration of partially hydrolyzed casein (amigen). J. Biol. Chem. 1946, 166: 649.
47. Clark, J. H., Nelson, W., Lyons, C., Mayerson, H. S., and DeCamp, P. Chronic shock; the problem of reduced blood volume in the chronically ill patient. Ann. Surg., 1947, 125: 618.
48. Coller, F. A., Campbell, K. N., Vaughan, H. H., Iob, V., and Moyer, C. A. Postoperative salt intolerance. Ann. Surg., 1944, 119: 533.
49. Coller, F. A., Iob, V., Vaughan, H. H., Kalder, N. B., and Moyer, C. A. Translocation of fluid produced by the intravenous administration of isotonic salt solutions in man postoperatively. Ann. Surg., 1945, 122: 663.
50. Cooper, D. R., Iob, V., and Coller, F. A. Response to parenteral glucose of normal kidneys and of kidneys of postoperative patients. Ann. Surg., 1949, 129: 1
51. Co Tui. Some clinical aspects of protein nutrition. J. Am. Diet. Ass., 1946, 22: 97.
52. Idem. Clinical experiences with oral use of protein hydrolysates. Ann. N. York Acad. Sc., 1946, 47: 359.
53. Co Tui, Kuo, N. H., Chuachiaco, M., and Mulholland, J. H. The protein depletion (hypoproteinemia) syndrome and its response to hyperproteinization. Anes. and Anal., 1949, 28: 1.
54. Co Tui, Kuo, H. H., Chuachiaco, M., Rosh, R., and Mulholland, J. H. Protein nutrition in cancer. Surg. Clin. N. America, 1949, 29: 449.
55. Co Tui, Wright, A. M., Mulholland, J. H., Carabba, V., Barcham, I., and Vinci, V. J. Studies on surgical convalescence; sources of nitrogen loss postgastrectomy and effect of high amino acid and high caloric intake on convalescence. Ann. Surg., 1944, 120: 99.
56. Cournand, A., Noble, R. P., Breed, E. S., Lawson, H. D., Baldwin, E. DeF., Pinchot, G. B., and Richards, D. W., Jr. Chemical, clinical and immunological studies on the products of human plasma fractionation; clinical use of concentrated human serum albumin in shock and comparison with whole blood and with rapid saline infusion. J. Clin. Invest., 1944, 23: 491.
57. Crook, C. E., Iob, V., and Coller, F. A. Correction of blood loss during surgical operations. Surg. Gyn. Obst., 1946, 82: 417.
58. Cuthbertson, D. P. The metabolism of proteins and amino acids. Ann. Rev. Biochem., 1947, 16: 153.
59. Idem. Assessment of knowledge concerning the clinical use of protein hydrolysates and pure amino acid mixtures. Am. J. Med., 1948, 6: 879.
60. Idem. The significance of proteins in nutrition; their particular importance during convalescence. Brit. M. J., 1948, 2: 731.
61. Davis, H. H. The administration of amino acids intravenously in surgical patients. Nebraska M. J., 1945, 30: 51.
62. DeCourcy, J. L. Significance of dietary supplementation in surgical cases. Am. J. Surg., 1949, 77: 461.
63. Dietrich, J. E., Whedon, G. D., and Shorr, E. Effects of immobilization upon the various metabolic and physiologic functions of normal men. Am. J. Med., 1948, 4: 3.
64. Eckhardt, R. D., Cooper, A. M., Faloon, W. W., and Davidson, C. S. Urinary excretion of amino acids in man. Tr. N. York Acad. Sc., 1948, 10: 284.
65. Eckhardt, R. D., Lewis, J. H., Murphy, T. L., Batchelor, W. H., and Davidson, C. S. Comparative studies on nutritive value of orally and intravenously administered human serum albumin in man. J. Clin. Invest., 1948, 27: 119.
66. Eckhardt, R. D., Zamchek, N., Sidman, R., and Gabuzda, G. Effect of protein starvation on the clinical course, liver function and liver histochemistry of patients with active liver disease. J. Clin. Invest., 1949, 28: 778.
67. Ellison, E. H., McCleery, R. S., Zollinger, R. M., and Case, C. T. The influence of caloric intake on the fate of parenteral nitrogen. Surgery, 1949, 26: 374.
68. Elman, R. Parenteral replacement of protein with amino acids of hydrolyzed casein. Ann. Surg., 1940, 112: 594.
69. Idem. Acute protein deficiency (hypoproteinemia) in surgical shock. J. Am. M. Ass., 1942, 120: 1176.
70. Idem. Maintenance of nitrogen balance by the intravenous administration of plasma proteins and protein hydrolysates. Physiol. Rev., 1944, 24: 372.
71. Idem. Parenteral Alimentation in Surgery. New York: Paul B. Hoeber, 1947.
72. Idem. Protein nutrition in surgery. N. York J. M., 1947, 47: 382.
73. Idem. Amino acid mixtures as parenteral protein food. Am. J. Med., 1948, 5: 760.
74. Idem. Parenteral feeding of protein. Arch. Surg., 1948, 57: 185.
75. Idem. Protein needs in surgery. Cincinnati J. M., 1948, 29: 680.
76. Elman, R., and Heifetz, C. V. Experimental hypoalbuminemia: its effect on morphology, function, and protein and water content of the liver. J. Exp. M., 1941, 73: 417.
77. Elman, R., Kelly, F. J., and Simonsen, D. H. Pure serum albumin compared with citrated plasma in the treatment of chronic hypoalbuminemia. Ann. Surg., 1948, 128: 195.
78. Elvehjem, C. A., and Krehl, W. H. Imbalance and dietary interrelationships in nutrition. J. Am. M. Ass., 1947, 135: 279.
79. Evans, E. I., and Bigger, I. A. The rationale of whole blood therapy in severe burns. Ann. Surg., 1945, 122: 693.
80. Evans, J. A., and Shulman, H. On the danger of forcing fluids in malnutrition. Am. J. M. Sc., 1940, 199: 237.
81. Fine, J., Hurwitz, A., and Mark, J. A clinical study of the plasma volume in acute intestinal obstruction. Ann. Surg., 1940, 112: 546.
82. Fink, R. M., Enns, T., Kimball, C. P., Silberstein, H. E., Bale, W. F., Madden, S. C., and Whipple, G. H. Plasma protein metabolism—normal and associated with shock. J. Exp. M., 1944, 80: 455.
83. Flink, E. B., and Skubi, K. B. Blood transfusion studies; survival of fresh and stored erythrocytes as determined by urobilinogen. J. Laborat. Clin. M., 1946, 31: 1074.
84. Food and Nutrition Board, National Research Council. Reprint and Circular Series No. 122, 1945.
85. Gamble, J. L. Physiological information gained from studies on the life raft ration. Harvey Lect., Balt., 1946–1947, 42: 247.

86. Geiger, E. Experiments with delayed supplementation of incomplete amino acid mixtures, J. Nutrit., 1947, 34: 97.
87. Idem. The role of the time factor in feeding supplementary proteins. J. Nutrit., 1948, 36: 813.
88. Gellis, S. S., Neefe, J. R., Stokes, J., Jr., Strong, L. E., and Scatchard, G. Inactivation of virus of homologous serum hepatitis in solutions of normal human serum albumin by means of heat. J. Clin. Invest., 1948, 27: 239.
89. Gibson, J. G., II, Aub, J. C., Evans, R. D., Peacock, W. C., Irvine, J. W., Jr., and Sack, T. Measurement of post-transfusion survival of preserved stored human erythrocytes by means of two isotopes of radioactive iron. J. Clin. Invest., 1947, 26: 704.
90. Gibson, J. G., II, and Evans, W. A., Jr. Clinical studies of the blood volume; relation of plasma and total blood volume to venous pressure, blood velocity rate, physical measurements, age and sex in 90 normal humans. J. Clin. Invest., 1937, 16: 317.
91. Gibson, J. G., II, Evans, R. D., Aub, J. C., Sack, T., and Peacock, W. C. Post-transfusion survival of preserved human erythrocytes stored as whole blood or in resuspension, after removal of plasma, by means of two isotopes of radioactive iron. J. Clin. Invest., 1947, 26: 715.
92. Gibson, S. T. Blood and its derivatives. N. England, J. M., 1948, 239: 544.
93. Goetsch, E., Lyttle, J. D., Grim, W. M., and Dunbar, P. Amino acid studies; reversibility of plasma amino acid during recovery from dietary hypoproteinemia in the dog. J. Biol. Chem., 1943, 151: 149.
94. Goldschmidt, S., Vars, H. M., and Ravdin, I. S. Influence of foodstuffs upon the susceptibility of liver to injury by chloroform and the probable mechanism of their action. J. Clin. Invest., 1939, 18: 277.
95. Greenfield, J., and Sanders, J. H. Total pancreatectomy with report of postoperative physiological studies. Surgery, 1949, 25: 824.
96. Gregersen, M. I. A practical method for the determination of plasma volume with the dye T-1824. J. Laborat. Clin. M., 1944, 29: 1266.
97. Griffin, G. E., Abbott, W. E., Pride, M. P., Muntwyler, E., Mautz, F. R., and Griffith, L. Plasma volume, "available (thiocyanate) volume" and total circulating plasma proteins in the normal adult. Ann. Surg., 1945, 121: 352.
98. Grossman, C. M., Sappington, T. S., Burrows, B. A., Lavietes, P. H., and Peters, J. P. Nitrogen metabolism in acute infections. J. Clin. Invest., 1945, 24: 523.
99. Guggenheim, K., and Buechler, E. Nutrition and resistance to infection; the effect of quantitative and qualitative protein deficiency on the bactericidal properties and phagocytic activity of the peritoneal fluid of rats. J. Immun., Balt., 1948, 58: 133.
100. Hall, C. A., and Drill, V. A. Relation of fat and protein intake to fatty changes, fibrosis, and necrosis of the liver. Proc. Soc. Exp. Biol. N. Y., 1949, 70: 202.
101. Hecht, H. H. Reactions to intravenously administered amino acids (casein hydrolysates). Am. J. M. Sc., 1946, 212: 351.
102. Hegsted, D. M., Hay, A. L., and Stare, F. J. Chemical, clinical and immunological studies on the products of human plasma fractionation; studies on the nutritive value of human plasma fractions. J. Clin. Invest., 1945, 24: 657.
103. Helfrick, F. W., and Abelson, N. M. Intravenous feeding of complete diet in child; report of case. J. Pediat., S. Louis, 1944, 25: 400.
104. Henschel, A., Mickelsen, O., Taylor, H. L., and Keys, A. Plasma volume and thiocyanate space in famine edema and recovery. Am. J. Physiol., 1947, 150: 170.
105. Himsworth, H. P. The Liver and Its Diseases. Cambridge: Harvard University Press, 1947.
106. Himsworth, H. P., and Glynn, L. E. Toxipathic and trophipathic hepatitis. Lancet, Lond., 1944, 246: 457.
107. Hirshfeld, J. W., Williams, H. H., Abbott, W. E., Heller, C. G., and Pilling, M. A. Significance of the nitrogen loss in the exudate from surface burns. Ann. Surg., 1944, 15: 766.
108. Hoffman, W. S. The clinical significance of proteins and amino acids in surgery. J. Internat. Coll. Surgeons, 1947, 10: 492.
109. Hoffman, W. S., Kozoll, D. D., Mok, W. T., Meyer, K. A., and Popper, H. Determination of the nitrogen balance index of a new lyophilized amino acid preparation in protein-deficient patients. J. Laborat. Clin. M., 1948, 33: 280.
110. Hollander, F., Rosenak, S., and Colp, R. A synthetic predigested aliment for jejunostomy feeding. Surgery, 1945, 17: 754.
111. Hollander F., and Sober, H. A. A modified synthetic predigested aliment for protracted jejunostomy feeding. Surgery, 1949, 25: 580.
112. Hollander, V., Chang, P., and Co Tui. Deuterium oxide and thiocyanate spaces in protein depletion. J. Laborat. Clin. M., 1949, 34: 680.
113. Homburger, F., and Young, N. F. Studies on hypoproteinemia; hypoproteinemia in patients with gastric cancer; its persistence after operation in the presence of body tissue repletion. Blood, N. Y., 1948, 3: 1460.
114. Howard, J. E., and Carey, H. A. The use of potassium in therapy. J. Clin. Endocr., 1949, 9: 691.
115. Howard, J. E., Duncan, L. E., Jr., and Meyer, R. J. Conf. on Metabolic Aspects of Convalescence. Josiah Macy, Jr. Foundation, 1948, 17: 46.
116. Janeway, C. A., Gibson, S. T., Woodruff, L. M., Heyl, J. T., Bailey, O. T., and Newhouser, L. R. Chemical, clinical and immunological studies on the products of human plasma fractionation; concentrated human serum albumin. J. Clin. Invest., 1944, 23: 465.
117. Johnson, J., Ravdin, I. S., Vars, H. M., and Zintel, H. A. Effect of diet on the composition of the liver in the presence of obstruction of the common bile duct. Arch. Surg., 1940, 40: 1104.
118. Johnson, R. M., Deuel, H. J., Jr., Morehouse, M. G., and Mehl, J. W. Effect of methionine upon urinary nitrogen in men at normal and low levels of protein intake. J. Nutrit., 1947, 33: 371.
119. Jones, C. M., and Eaton, F. B. Postoperative nutritional edema. Arch. Surg., 1933, 27: 159.
120. Keeton, R. W., Cole, W. H., Calloway, N., Glickman, N., Mitchell, H. H., Dyniewicz, J., and Howes, D. Convalescence; a study in the physiological recovery of nitrogen metabolism and liver function. Ann. Int. M., 1948, 28: 521.
121. Keeton, R. W., and Dickson, D. Excretion of nitrogen by obese patients on diets low in calories containing varying amounts of protein. Arch. Int. M., 1933, 51: 890.

122. KEYS, A., TAYLOR, H. L., MICKELSEN, O., and HENSCHEL, A. Famine edema and mechanism of its formation. Science, 1946, 103: 669.
123. KINSELL, L. W., MARGEN, S., TARVER, H., FRANTZ, J. McB., and FLANAGAN, E. K. Studies in protein metabolism with the aid of S^{35} labelled methionine. J. Clin. Invest., 1949, 28: 793.
124. KINSELL, L. W., MICHAELS, G. D., BARTON, H. C., and WEISS, H. A. Protein balance studies in patients with liver damage; role of lipotropic agents. Ann. Int. M., 1948, 29: 881.
125. KOSTER, H., and KASMAN, L. P. Relation of serum proteins to well healed and to disrupted wounds. Arch. Surg., 1942, 45: 776.
126. KOSTER, H., and SHAPIRO, A. Serum proteins and wound healing. Arch. Surg., 1940, 41: 723.
127. KOSTERLITZ, H. W. The effects of changes in dietary protein on the composition and structure of the liver cell. J. Physiol., 1947, 106: 194.
128. KOZOLL, D. D., HOFFMAN, W. S., and MEYER, K. A. Nitrogen balance studies on surgical patients receiving amino acids. Arch. Surg., 1945, 51: 59.
129. KOZOLL, D. D., HOFFMAN, W. S., MEYER, K. A., and GARVIN, T. High protein therapy; clinical effectiveness of oral administration of a new protein preparation as determined by nitrogen balance studies. Arch. Surg., 1946, 53: 683.
130. KOZOLL, D. D., and MOK, W. T. Studies in nitrogen metabolism. J. Laborat. Clin. M., 1947, 32: 1403.
131. KREMEN, A. Problems of parenteral nitrogen administration in surgical patients; with special consideration of preoperative preparation and of effecting favorable nitrogen balance. Surgery, 1948, 23: 92.
132. LENAHAN, N. E., SPITZ, T. A., and METCALF, D. W. Blood determination and estimation of blood loss during operations. Arch. Surg., 1948, 57: 435.
133. LEVENSON, S. M., BIRKHILL, F. R., MALONEY, M. A., and BELL, T. A. Metabolic fate of the infused erythrocyte. Ann. Surg., 1949, 130: 723.
134. LEVERTON, R. M., SCHLAPHOFF, D., and HUFFSTETTER, M. Blood regeneration in women blood donors; effect of protein, mineral, and vitamin supplements. J. Am. Diet. Ass., 1948, 24: 480.
135. LEWIS, J. H., TAYLOR, F. H. L., and DAVIDSON, C. S. Tolerance to intravenously administered protein hydrolysates in severe human liver cirhosis. Am. J. M. Sc., 1947, 214: 656.
136. LI, T., and FREEMAN, S. Effect of protein deficiency and cholesterol feeding on the liver of dogs. Am. J. Physiol., 1946, 145: 646.
137. LOCALIO, S. A., CHASSIN, J. L., and HINTON J. W. Tissue protein depletion; a factor in wound disruption. Surg. Gyn. Obst., 1948, 86: 147.
138. LOCALIO, S. A., MORGAN, M. E., and HINTON, J. W. The biological chemistry of wound healing; the effect of dl-methionine on the healing of wounds in protein-depleted animals. Surg. Gyn. Obst., 1948, 86: 582.
139. LOCKWOOD, J. S., and RANDALL, H. T. The place of electrolyte studies in surgical patients. Bull. N. York Acad., 1949, 25: 228.
140. LOWELL, A., COURNAND, A., and RICHARDS, D. W., JR. Changes in plasma volume and mean arterial pressure after intravenous injection of concentrated human serum albumin in 38 patients with oligemia and hypotension. Surgery, 1947, 22: 442.
141. LUCK, J. M. Liver Proteins. In Perspectives in Biochemistry by J., Needham, and D. E. GREEN New York: Macmillan Co., 1937.
142. LUND, C. C. The protein nutrition of surgical patients. Surg. Gyn. Obst., 1946, 83: 259.
143. LUND, C. C., and LEVENSON, S. M. Proteins in surgery. J. Am. M. Ass., 1945, 128: 95.
144. LYON, R. P., STANTON, J. R., FREIS, E. D., and SMITHWICK, R. H. Blood volume and "available fluid" (thiocyanate) volume studies in surgical patients; normal patterns of response of the blood volume, available fluid, protein, chloride, and hematocrit in the postoperative surgical patient. Surg. Gyn. Obst., 1949, 89: 9.
145. MACHELLA, T. Hyperalimentation in the treatment of chronic idiopathic ulcerative colitis. Am. J. Med., 1949, 7: 191.
146. MADDEN, S. C., BASSETT, S. H., REMINGTON, J. H., MARTIN, F. J. C., WOODS, R. R., and SHULL, F. W. Amino acids in therapy of disease (parenteral and oral administration compared). Surg. Gyn. Obst., 1946, 82: 131.
147. MADDEN, S. C., KATTUS, A. A., JR., CARTER, J. R., MILLER, L. L., and WHIPPLE, G. H. Plasma protein production as influenced by parenteral protein digests, very high protein feeding, and red blood cell catabolism. J. Exp. M., 1945, 82: 181.
148. MADDEN, S. C., and WHIPPLE, G. H. Amino acids in the production of plasma protein and nitrogen balance. Am. J. M. Sc., 1946, 211: 149.
149. MADDEN, S. C., and WHIPPLE, G. H. Plasma proteins; their source, production, and utilization. Physiol. Rev., 1940, 20: 194.
150. MADDEN, S. C., WINSLOW, P. M., HOWLAND, J. W., and WHIPPLE, G. H. Blood plasma protein regeneration as influenced by infection, digestive disturbances, thyroid, and food proteins; deficiency state related to protein depletion. J. Exp. M., 1937, 65: 431.
151. MAN, E. B., BETTCHER, P. G., CAMERON, C. M., and PETERS, J. P. Plasma alpha-amino acid nitrogen and serum lipids of surgical patients. J. Clin. Invest., 1946, 25: 701.
152. MANN, G. V., GEYER, R. P., WATKIN, D. M., SMYTHE, R. L., DJU, D., ZAMCHEK, N., and STARE, F. J. Parenteral nutrition; metabolic studies on puppies infused with fat emulsions. J. Laborat. Clin. M., 1948, 33: 1503.
153. MAUTZ, F. R. Nutritional problems in surgical patients with special reference to depletion of plasma protein reserves. Ohio M. J., 1948, 44: 1217.
154. MECRAY, P. M., BARDEN, R. P., and RAVDIN, I. S. Nutritional edema; its effect on gastric emptying time before and after gastric operations. Surgery, 1937, 1: 53.
155. MENG, H. C. Study of complete parenteral alimentation in dogs. Am. J. Med., 1949, 7: 244.
156. METCOFF, J., FAVOUR, C. B., and STARE, F. J. Plasma protein and hemoglobin in the protein deficient rat. J. Clin. Invest., 1945, 24: 82.
157. METCOFF, J., and STARE, F. J. The physiologic and clinical significance of plasma proteins and protein metabolites. N. England J. M., 1947, 236: 26.
158. MEYER, F. L., HIRSHFELD, J. W., ABBOTT, W. E., PILLING, M. A., WILLIAMS, H. H., and RICHARDS, A. J. Nitrogen balance and blood volume studies on man during and following repeated plasma transfusions. Am. J. M. Sc., 1947, 213: 160.
159. MILLER, L. L., ROBSCHEIT-ROBBINS, F. S., and WHIPPLE, G. H. Anemia and hypoproteinemia; weight maintenance effected by food proteins but not by mixtures of pure amino acids. J. Exp. M., 1947, 85: 267.

160. MILLER, L. L., ROSS, J. F., and WHIPPLE, G. H. Methionine and cystine, specific protein factors preventing chloroform liver injury in protein depleted dogs. Am. J. M. Sc., 1940, 200: 739.
161. MILLER, L. L., and WHIPPLE, G. H. Chloroform liver injury increases as protein stores decrease. Am. J. M. Sc., 1940, 199: 204.
162. MOK, W. T., KOZOLL, D. D., and MEYER, K. A. Studies in nitrogen metabolism. Surgery, 1948, 24: 952.
163. MOLLISON, P. L., and YOUNG, I. M. On the survival of transfused erythrocytes of stored blood. Q. J. Exp. Physiol., Lond., 1941, 30: 313.
164. Idem. In vivo survival in human subjects of transfused erythrocytes after storage in various preservative solutions. Q. J. Exp. Physiol., Lond., 1942, 31: 359.
165. MOORE, F. D. Surgical nutrition. Nutrit. Rev., 1948, 6: 161.
166. MOORE, N. S. Parenteral nutrition; protein privation. N. York M. J., 1949, 49: 492.
167. MOORE, N. S., and VAN SLYKE, D. D. The relationship between plasma specific gravity, plasma protein content and edema in nephritis. J. Clin. Invest., 1930, 8: 337.
168. MULHOLLAND, J. H., CO TUI, WRIGHT, A. M., VINCI, V., and SHAFIROFF, B. Protein metabolism and bed sores. Ann. Surg., 1943, 118: 1015.
169. OELGOETZ, A. W., OELGOETZ, P. A., and WITTEKIND, J. Protein insufficiency of clinical importance in surgery upon liver. Ohio M. J., 1937, 33: 643.
170. ORTEN, A. V., and ORTEN, J. M. Dietary protein in hemoglobin formation. J. Nutrit., 1943, 26: 21.
171. Idem. Comparative value of certain dietary proteins for hemopoiesis in rat. J. Nutrit., 1946, 31: 765.
172. PAULSON, M. Gastroenterology, 1946, 7: 448.
173. PETERS, J. P. Symposium on the fluid and electrolyte needs of the surgical patient; structure of blood in relation to surgical problems. Ann. Surg., 1940, 112: 490.
174. Idem. Effect of injury and disease on nitrogen metabolism. Am. J. Med., 1948, 5: 100.
175. PRIESTLEY, J. T., COMFORT, M. W., and SPRAGUE, R. G. Total pancreatectomy for hyperinsulinism due to islet-cell adenoma. Ann. Surg., 1949, 130: 211.
176. RASMUSSEN, L. H., ABELS, J. C., PACK, G. T., and RHOADS, C. P. Effect of high protein diet on the prevention of postoperative hypoproteinemia in patients with gastric cancer. J. Am. M. Ass., 1944, 124: 358.
177. RAVDIN, I. S. Hypoproteinemia and its relation to surgical problems. Ann. Surg., 1940, 112: 576.
178. Idem. Protein deficiency in surgical patients. Surg. Clin. N. America, 1946, 26: 1306.
179. Idem. Surgical jaundice; factors influencing injury and repair of the liver. Surg. Gyn. Obst., Internat. Abstr. Surg., 1949, 89: 209.
180. RAVDIN, I. S., MCNAMEE, H. G., KAMHOLZ, J. H. and RHOADS, J. E. Effect of hypoproteinemia on susceptibility to shock resulting from hemorrhage. Arch. Surg., 1944, 48: 491.
181. RAVDIN, I. S., STENGEL, A., JR., and PRUSHANKIN, M. Control of hypoproteinemia in surgical patients. J. Am. M. Ass., 1940, 114: 107.
182. RAVDIN, I. S., THOROGOOD, E., RIEGEL, C., PETERS, R., RHOADS, J. E. The prevention of liver damage and the facilitation of repair of the liver by diet. J. Am. M. Ass., 1943, 121: 322.
183. REMINGTON, J. H. Amino acid alimentation in gastrointestinal disease. Gastroenterology, 1946, 7: 442.
184. RHOADS, J. E., and KASINSKAS, W. Influence of hypoproteinemia on the formation of callus in experimental fracture. Surgery, 1942, 11: 38.
185. RIEGEL, C., KOOP, C. E., DREW, J., STEVENS, L. W., and RHOADS, J. E. Nutritional requirements for nitrogen balance in surgical patients in early postoperative period. J. Clin. Invest., 1947, 26: 18.
186. RIEGEL, C., KOOP, C. E., SCHWEGMAN, C. W., BARNES, M. T., and GRIGGER, R. P. An evaluation of mixtures of ossein gelatin, hydrolyzed protein and glucose in the parenteral nutrition of postoperative patients. Surgery, 1949, 25: 672.
187. RISSER, W. C., SCHENCK, J. R., and FROST, D. V. Intravenous utilization of partial acid hydrolysates of proteins. J. Nutrit., 1946, 32: 499.
188. ROBSCHEIT-ROBBINS, F. S., MILLER, L. L., and WHIPPLE, G. H. Hemoglobin and plasma protein production; various proteins, concentrates and digests influence blood protein production in anemia and hypoproteinemia. J. Exp. M., 1946, 83: 463.
189. ROBSCHEIT-ROBBINS, F. S., and WHIPPLE, G. H. Dietary effects on anemia plus hypoproteinemia in dogs; some proteins further the production of hemoglobin and others, plasma protein production. J. Exp. M., 1949, 89: 339.
190. Idem. The findings with milk products, wheat, and peanut flour as compared with liver. J. Exp. M., 1949, 89: 359.
191. ROSE, C. S., MACHELLA, T. E., and GYORGY, P. Absence of lipotropic activity of methionine when pure amino acids were substituted for dietary protein. Proc. Soc. Exp. Biol., N. Y. 1947, 64: 352.
192. ROSE, W. C. Nutritive significance of amino acids. Physiol. Rev., 1938, 18: 109.
193. ROSE, W. C., HAINES, W. J., JOHNSON, J. E., and WARNER, D. T. Further experiments on the role of amino acids in human nutrition. J. Biol. Chem., 1943, 148: 457.
194. SACHAR, L. A., HORVITZ, A., and ELMAN, R. Studies on hypoalbuminemia produced by protein deficient diets; hypoalbuminemia as a quantitative measure of tissue protein depletion. J. Exp. M., 1942, 75: 453.
195. SAHYUN, M. Methionine. Am. J. Digest. Dis., 1949, 16: 248.
196. SCATCHARD, G., BATCHELDER, A. C., and BROWN, A. Chemical, clinical, and immunological studies on the products of human plasma fractionation; osmotic pressure of plasma and serum albumin. J. Clin. Invest., 1944, 23: 458.
197. SCATCHARD, G., STRONG, L. E., HUGHES, W. L., JR., ASHWORTH, J. N., and SPARROW, A. H. Chemical, clinical, and immunological studies on the products of human plasma fractionation; properties of solutions of human serum albumin of low salt content. J. Clin. Invest., 1945, 24: 671.
198. SCHEINBERG, I. H., KINNEY, T. D., and JANEWAY, C. A. Homologous serum jaundice. J. Am. M. Ass., 1947, 134: 841.
199. SCHOENHEIMER, R. The Dynamic State of Body Constituents. Cambridge: Harvard University Press, 1946.
200. SCHWIMMER, D., and MCGAVACK, T. H. Some newer aspects of protein metabolism. N. York M. J., 1948, 48: 1797.
201. SELYE, H. Studies on adaptation. Endocrinology, 1937, 21: 169.

202. SHAFIROFF, B. G. P., MULHOLLAND, J. H., CO TUI, ROTH, E., and BARON, H. C. The intravenous administration of a combined fat emulsion into surgical patients. Surg. Gyn. Obst., 1949, 89: 398.
203. SILBER, R. H., HOWE, E. E., and PORTER, C. C. Utilization of amino acid mixtures by dogs. Tr. N. York Acad. Sc., 1948, 10: 277.
204. SMYTH, C. J., LEVEY, S., and LASICHAK, A. G. The relationship of glutamic and aspartic acids to the production of nausea and vomitting in man. Am. J. M. Sc., 1947, 214: 281.
205. SPURLING, N., SHONE, J., and VAUGHAN, J. Incidence, incubation period and symptomatology of homologous serum jaundice. Brit. M. J., 1946, 2: 409.
206. STANTON, J. R., LYON, R. P., FREIS, E. D., and SMITHWICK, R. H. Blood and "available fluid" (thiocyanate) volume studies in surgical patients; operative and postoperative blood loss with particular emphasis upon uncompensated red cell loss. Surg. Gyn. Obst., 1949, 89: 181.
207. STARE, F. J., and DAVIDSON, C. S. Protein; its role in human nutrition. J. Am. M. Ass., 1945, 127: 985.
208. STARE, F. J., and THORN, G. W. Protein nutrition in problems of medical interest. J. Am. M. Ass., 1945, 127: 1120.
209. STEWART, J. D., HALE, H. W., and SCHAER, S. M. Management of protein deficiency in surgical patients. J. Am. M. Ass., 1948, 136: 1017.
210. STRUMIA, M. M., BLAKE, A. D., REIDER, H. C., and CHORNOCK, F. W. Use of "modified globin" from human erythrocytes in hypoproteinemias. Am. J. M. Sc., 1946, 211: 51.
211. STUDLEY, H. O. Percentage of weight loss: a basic indicator of surgical risk in patients with chronic peptic ulcer. J. Am. M. Ass., 1936, 106: 458.
212. TAGNON, H. J., ROBBINS, G. F., and NICHOLS, M. P. The effect of surgical operations on the bromsulfalein-retention test. N. England J. M., 1948, 238: 556.
213. TAYLOR, H. L., MICKELSEN, O., and KEYS, A. The effects of induced malaria, acute starvation and semi-starvation on the electrophoretic diagram of the serum proteins of normal young men. J. Clin. Invest., 1949, 28: 273.
214. THALHIMER, W., and TAYLOR, E. S. The transfusion of centrifuged human type O cells; resuspended and stored in 10 per cent corn syrup. J. Am. M. Ass., 1945, 127: 1096.
215. THOMPSON, W. D., RAVDIN, I. S., and FRANK, I. L. Effect of hypoproteinemia on wound disruption. Arch. Surg., 1938, 36: 500.
216. VAN SLYKE, D. D. Physiology of the amino acids. Science, 1942, 95: 259.
217. VARCO, R. L. Preoperative dietary management for surgical patients with special reference to lesions of the stomach and duodenum. Surgery, 1946, 19: 303.
218. Idem. Nutritional preparation for substandard risk patients. Surg. Gyn. Obst., 1947, 84: 611.
219. WANG, C., HEGSTED, D. M., LAPI, A., ZAMCHEK, N., and BLACK, M. B. Progressive changes in liver composition, function, body fluids, and liver cytology during protein depletion in the rat and the effect of choline upon these changes. J. Laborat. Clin. M., 1949, 34: 953.
220. WANG, C., LAPI, A., and HEGSTED, D. M. Studies on minimum protein requirements of adult dogs. J. Laborat. Clin. M., 1948, 33: 462.
221. WANGENSTEEN, O. H. Controlled administration of fluid to surgical patients including a description of gravimetric methods of determining the status of hydration and blood loss during operation. Minnesota M., 1942, 25: 783.
222. WATERHOUSE, C., BASSETT, S. H., and HOLLER, J. W. Metabolic studies on protein-depleted patients receiving a large part of their nitrogen intake from human serum albumin administered intravenously. J. Clin. Invest., 1949, 28: 245.
223. WEECH, A. A. The significance of the albumin fraction of serum. Harvey Lect., Balt., 1938–1939, 34: 57.
224. WEECH, A. A., WOLLSTEIN, M., and GOETTSCH, E. Nutritional edema in the dog; development of deficits in erythrocytes and hemoglobin on a diet deficient in protein. J. Clin. Invest., 1937, 16: 719.
225. WERNER, S. C. The use of a mixture of pure amino acids in surgical nutrition. Ann. Surg., 1947, 126: 169.
226. Idem. Problems of parenteral nutrition. Am. J. Med., 1948, 5: 749.
227. WERNER, S. C., HABIF, D. Y., RANDALL, H. T., and LOCKWOOD, J. S. Postoperative nitrogen loss; a comparison of the effects of trauma and caloric readjustment. Ann. Surg., 1949, 130: 688.
228. WHEDON, G. D., DIETRICK, J. E., and SHORR, E. Modification of the effects of immobilization upon the metabolic and physiologic functions of normal men by the use of an oscillating bed. Am. J. Med., 1949, 6: 684.
229. WHIPPLE, A. O. Determining factors in the safety and success of radical, present-day surgery. Surgery, 1949, 25: 169.
230. WHIPPLE, G. H., and MADDEN, S. C. Hemoglobin, plasma proteins and cell proteins; their interchange and construction in emergencies. Medicine, Balt., 1944, 23: 215.
231. WHIPPLE, G. H., MILLER, L. L., and ROBSCHEIT-ROBBINS, F. S. Raiding of body tissue protein to form plasma protein and hemoglobin. J. Exp. M., 1947, 85: 277.
232. WILEY, H. M. Postoperative protein deficiency, with special reference to the cancer patient. Surgery, 1947, 21: 889.
233. WOLF, A. M., MASON, J., FITZPATRICK, W. J. SCHWARTZ, S. O., and LEVINSON, S. O. Ultraviolet irradiation of human plasma as a means of controlling homologous serum jaundice. J. Am. M. Ass., 1947, 135: 476.
234. WOMACK, M., and ROSE, W. C. Evidence for the existence of an unidentified growth stimulant in proteins. J. Biol. Chem., 1946, 162: 735.
235. WOOLEY, D. W. Some correlations of growth promoting powers of proteins with their strepogenin content. J. Biol. Chem., 1946, 162: 383.
236. YOUMANS, J. B. The clinical detection of protein deficiency. J. Am. M. Ass., 1945, 128: 439.

ABSTRACTS OF CURRENT LITERATURE

SURGERY OF THE HEAD AND NECK

HEAD

Salivary Gland Tumors of the Submaxillary Gland Associated with Calculi. EPHRAIM L. MANNING and MAURICE A. MICHAEL. *Ann. Otol. Rhinol.*, 1950, 59: 141.

Two cases of enlargement of the submaxillary salivary glands are presented. In each, an original diagnosis of salivary calculus was made and at operation, in addition to the calculus, a mixed tumor was found. The authors emphasize that the possibility of tumor must always be considered in such cases.

JOHN J. BALLENGER, M.D.

EYE

The Exploration of the Orbit. W. HEDLEY SUMMERSKILL. *Brit. J. Ophth.*, 1950, 34: 292.

Exploration of the orbit is discussed, and the author states that space-occupying lesions in the orbit can be diagnosed fairly accurately. However, determination of the nature, the size, and the exact position of such tumors is difficult. Tumors near the outlet of the orbit and those outside the periorbita present little difficulty, but when deeper tumors in the intermediate space and in the muscle cone are present, the surgical procedure is to some extent exploratory. For these cases a subperiorbital approach is usually adopted following either a Kronlein osteoplastic resection or incision down to the orbit.

A modification of the transconjunctival route advocated by Reese and others is preferred, and this procedure was followed in a series of 8 consecutive cases, in 7 of which intraorbital tumors were found. In this procedure a free lateral canthotomy is made and the lateral palpebral ligament and the palpebral fascia are freed from their attachment to the periosteum. The horizontal incision in the conjunctiva is extended upwards or downwards as necessary, keeping a few millimeters to the bulbar side of the fornix. If it is desired to explore the inner side of the orbit, the incision is continued round to the internal rectus. This procedure permits digital palpation through the incision, to investigate the contents of the muscle cone and of the intermediate space to be examined.

If the tumor is in the intermediate space, the conjunctival incision is extended as required. If more room is required the rectus muscle may be sectioned and the eye displaced.

Summerskill is of the opinion that a transconjunctival approach combined with a free canthotomy is a satisfactory method for exposing the orbit and dealing with any lesion that may be found. Its chief advantages are:

1. It provides access to every part of the orbit so that removal of any mass may be thoroughly effected. This is also true of even some benign tumors, recurrence of which may be malignant.
2. It results in only slight, if any, postoperative deformity or disfigurement. For this reason there should be little hesitation in exploring any orbit suspected of containing a tumor, the exact diagnosis of which is doubtful.
3. It does not jeopardize the efficient performance of any further surgical or other procedure which may be required by the condition discovered. Small intraorbital tumors can be readily removed, the conjunctival incision can be extended, and the muscles pushed aside or even resected to permit access to any part of the orbit. With a transconjunctival approach, no incision is made through the periorbita, so that if malignant disease is revealed the contents of the orbit can be exenterated within an intact periosteal sac. JOSHUA ZUCKERMAN, M.D.

Transplantation of the Lacrimal Glands in Man and Rat; Effect of Injury of the Lacrimal Duct in the Rat. Clinical and Experimental Study. MAUNO VANNAS. *Arch. Ophth.*, Chic., 1950, 43: 804.

Vannas had found that transplantation of two-thirds of the palpebral gland from healthy patients with epiphora to patients with severe xerophthalmos incident to old trachoma was of moderate benefit in one of three eyes. In the hope of improving his results he studied the grafting of the lacrimal gland in adult albino rats under controlled experimental conditions.

The results in 46 autotransplantations and homeotransplantations indicate that the exchange of parts of lacrimal glands in the same animal from one side to the other was far better tolerated than was homeotransplantation. In contrast to the human eye, surgical grafting of the lacrimal gland of the rat often led to severe complications in the eye. Autotransplantations were less injurious to the sensitive rat eye than were homeotransplantations.

JAMES E. LEBENSOHN, M.D.

Ocular Fat Embolism. A Clinical and Pathologic Report. ARTHUR GERARD DEVOE. *Arch. Ophth.*, Chic, 1950, 43: 857.

Ocular fat embolism is not so rare as has been thought, though it is distinctly unusual. Fracture of one or more of the long bones is oftenest the chief traumatic lesion. It is assumed that the fat of the bone marrow enters the venous system through torn, open veins.

In the case presented, the fundus was observed before death and a complete necropsy was per-

formed. A man, aged 25, was struck by an automobile and received multiple compound fractures of both tibias and fibulas, fractures of the right eleventh rib, and of the transverse processes of the first to fourth lumbar vertebrae. He became comatose and cyanotic the next day. The pupils were pin-point and the eyeballs occasionally rolled irregularly. Numerous petechial hemorrhages, present in the skin, were also seen in the palpebral and bulbar conjunctivae. The eyes were examined 18 hours before death, which occurred 2½ days after the injury.

In each fundus a typical cherry red spot was present at the macula, surrounded by an area of edema. Adjacent to this were discrete fluffy exudates of the cotton wool type. No hemorrhages were present.

Autopsy showed venous engorgement and fresh interstitial hemorrhages in all organs. Staining revealed massive fat embolism of the capillaries and venules in all organs, as well as fat globules within the alveoli of the lung and the lumens of the renal tubules. Histologic study of the eyes showed no abnormalities of the cornea, iris, chamber angle, or ciliary body. Throughout the extent of the choroid, but most conspicuously at the posterior pole, globules of fat were irregularly encountered. The retina likewise presented numerous vessels occluded with fat, which were often surrounded by patches of disorganized, edematous retina. The nerve heads were normal, but fat was present in the vessels of the optic nerve. JAMES E. LEBENSOHN, M.D.

Hereditary and Constitutional Dystrophies of the Cornea. WILLIAM B. CLARK. *Am. J. Ophth.*, 1950, 33: 692.

The familial character of the hereditary corneal dystrophies was first noted by Fuchs in 1901. The dystrophies are rare in brown-eyed individuals and no case has yet been reported in negroes. They are not associated with any other known disease and are not amenable to any form of curative therapy. In all these diseases the affection is bilateral and the onset occurs in the first decade of life; the nodules cause irregularity of the corneal surface and attacks of pain are common; the central area of the cornea is affected primarily and vascularization is absent. These dystrophies are not common, but should be remembered in the diagnosis of obscure lesions.

Recent studies have demonstrated that there are three distinctive types of hereditary corneal dystrophy. The transmission is dominant in the granular and reticular forms, and recessive in the macular type, where a background of consanguinity is common. The eponyms previously attached to these conditions will soon become obsolescent.

In granular corneal dystrophy (Groenouw's Type I) the sharply demarcated irregular spots suggest by their outline crumbs of bread. Corneal sensation is usually normal. Vision deteriorates, but very slowly. In cases with recurring erosions the mistaken diagnosis of herpes is frequently made.

In reticular corneal dystrophy (Haab-Dimmer type), opaque interlocking lines and nodules are observed. Slit-lamp examination shows the linear opacities to be characteristically double-contoured, and most prominent peripheral to the central zone, but the extreme marginal zone remains free. Corneal sensation is greatly impaired. Visual acuity decreases at an early age. Recurring corneal erosions are common.

In macular corneal dystrophy (Groenouw's Type II), the numerous spots form a diffuse opacity over the whole area. Corneal sensitivity is extremely diminished, but the epithelium is not much affected. Blindness is usual by the age of 30.

JAMES E. LEBENSOHN, M.D.

Dystrophies of the Cornea. The Fifth Sanford R. Gifford Lecture. EVERETT L. GOAR. *Am. J. Ophth.*, 1950, 33: 674.

The six principal types of corneal dystrophy are critically reviewed and lavishly illustrated.

Primary fatty or lipoid degeneration. With failure in the enzymatic oxidation of lipoids, fat accumulates in and between the cells. This sets up a foreign-body reaction; macrophages phagocytose the fat and are transformed into foam cells. Exudation and fibrosis ensue. Somewhat related to this group are the corneal opacities, stationary in character, uniformly found in gargoylism.

Marginal dystrophy. The flattening of the cornea in the region of greatest involvement results in high astigmatism. The disease progresses very slowly until finally Descemet's membrane bulges through the furrow.

Primary band-shaped or zonular dystrophy. The opacity begins at the limbus margins in the interpalpebral fissure and moves slowly across the cornea. Bowman's membrane shows a characteristic calcification, and dark holes are seen with the slit-lamp where corneal nerve fibers emerge—a pathognomonic finding. Superficial keratectomy may improve vision.

Salzmann's nodular dystrophy. Though this dystrophy follows phlyctenular keratitis, the nodules are of degenerative nature and the hypertrophic scar formation is similar to that in keloid. The disease is commonest in females, is often unilateral, and not familial.

Familial hereditary dystrophies. The commonest form is the granular type, which always shows clear cornea in the periphery and between the opacities. The second commonest type is macular corneal dystrophy, a recessive form, that may show up unexpectedly in children of healthy parents. The rarest form is reticular dystrophy ("lattice keratitis").

Endothelial dystrophy. This condition is always bilateral, and is most often marked in women of the fifth decade, but about 6 per cent of all patients are affected to some degree. Hyperactivity of the endothelium induces excrescences in Descemet's membrane, which become more numerous when the condition is progressive. Epithelial dystrophy follows

when in rare cases the integrity of the aqueous barrier is destroyed and the epithelial cells become waterlogged and break down. A corneal transplant is ineffective as it soon assumes the characteristics of the host's cornea. JAMES E. LEBENSOHN, M.D.

International Symposium on Corneal Surgery. R. TOWNLEY PATON, J. I. BARRAQUER, JR., G. P. SOURDILLE, JAMES E. ROBERTS, and Others. *Am. J. Ophth.*, 1950, 33: 3.

In this international symposium a number of ophthalmologists discuss various aspects of corneal surgery with special reference to corneal transplantation.

PATON presented a foreword on the Eye Bank for Sight Restoration and expressed the hope that the exchange of knowledge about keratoplasty would advance the service of ophthalmology in the alleviation of blindness throughout the world.

He also presented a historical review of corneal transplantation, referring to the contributions by Pellier de Quengsy (1789), Autenrieth (1814), Schmidt (1814), Beer (1814), Gertner (1817), Riecke (1823), Meissner (1823), Reisinger (1818), Himly (1813), Stilling (1836), Koenigshoefer (1836) Strauch (1841), Markus (1841), Steinberg (1843), Von Hippel (1877), Zirm (1907), Elschnig (1908), and Filatov (1922). He pointed out that the most interesting development at present is the use of the nonpenetrating corneal transplant for therapeutic purposes.

Barraquer described his technique of penetrating keratoplasty. He pointed out that the postoperative complications which usually result from poor coaptation of the graft include: displacement of the graft, infection, edema, delay in the formation of the anterior chamber, anterior synechiae, iris prolapse, hypotrophy, hypertension, keratitis, hemorrhage, iridocyclitis, vascularization, and dystrophia.

It should be emphasized that not only must the most suitably sized graft (preferably between 5.0 and 6.5 mm.) be determined for each case but also that the graft must be absolutely centered with the pupil, and that it has to border on cornea of normal thickness.

If the cornea is very thick (in total leucomas), a superficial keratoplasty has to be performed to thin out and improve the bed. This procedure is superior to keratectomy.

Penetrating keratoplasty with round grafts of a size similar to that of the resection was generally used. The trephine has a central pin and is used like a carpenter's center bit.

The operative procedure is as follows: the pupil is kept in miosis with eserine because miosis has certain advantages; it permits more perfect centering of the graft with the pupil, greater cleanness of trephination because of better visibility of the chamber depth, better protection of the lens and better visibility if the trephination should have to be completed with a different instrument, less danger of the formation of anterior synechiae (particularly sphincteric ones which occur most frequently and are most serious), and the pupil will not contract when the anterior chamber is opened.

The following sequence is observed: akinesia of the orbicularis, retrobulbar injection, trephination, obtaining the graft, placing the graft, and suturing. The trephination is performed 2 minutes after the retrobulbar injection. A longer delay would necessitate operation on a hypotonic eye with danger to the uniformity of the section.

The graft is obtained preferably from an adult cornea taken immediately after death and preserved for not more than 3 days in the refrigerator, in moist air, and at a temperature between 2° and 4°C.

The suturing of the graft is considered the most important step in the operation because most postoperative troubles are due to faulty or incorrect fixation. Direct suturing of the graft with fine silk thread and sharp needles (5 mm. long and with a radius of curvature of 5 mm.) and with a downward cutting edge insures the best results. The sutures must go through one-half of the thickness of the parenchyma in larger or smaller number according to the diameter of the transplant and the conditions in each case.

The patient is kept in bed for 12 days but may sit up whenever he wishes.

At the first dressing on the third or fourth day, an atropine collyrium (2.5 per cent) is instilled. Dressings are renewed every 2 or 3 days. On the fourth day, a saline aperient or mild laxative may be prescribed. After 10 days a monocular dressing is applied and the patient allowed up. The sutures are removed in about 14 days. The dressing may be removed after 17 days in 5.0 mm. trephinations; after 20 days in 6.0 mm. trephinations; and after 22 days in trephinations of 6.5 mm.

Mydriasis (never miosis) must be maintained if the slightest reaction (hyperemia or photophobia) is present. In cases of increased intraocular tension, a cyclodialysis or an Elliot trephining operation may be performed and mydriasis should be continued.

If the suturing needles are not extremely sharp, it is better to place a bridging suture, even though the results will be less certain.

The excellent results obtained with this technique are shown by the high percentage of transparencies, by the absence of postoperative complications, and by the absence of a limiting ring.

SOURDILLE discussed the complications of keratoplasty as well as their prevention and treatment.

The technical errors during operation include mistakes in placing the graft, oblique resection of the cornea with resultant displacement and scarring, inefficient section of the layers of the graft, and misplacing of corneal sutures.

The postoperative complications following penetrating keratoplasty are: displacement of the graft, deformity of the graft, adhesions between the graft and the iris, and secondary glaucoma.

In complicated cases the prognosis is very different. Preliminary operations should be performed to

correct extensive vascularized leucomas, anterior synechiae, and symblepharon or defects of the eyelids. Vascularization may produce serious consequences.

If, several days after the operation, some new vessels are seen in the graft, roentgen ray treatment should be given. The earlier this treatment is started the better will be the results. The usual treatment consists of 50 roentgens. A total of from 200 to 250 roentgens may be sufficient to arrest vascular invasion of the graft.

ROBERTS presented statistics in 100 cases of partial penetrating keratoplasty in relation to the clarity of the transplanted corneal tissue.

Without selection of cases it was found that there was better than one chance in two that the graft would remain clear.

The actual findings were as follows: 55 per cent of the grafts were clear and 45 per cent cloudy. With proper selection of cases, a higher percentage of clear grafts should be obtained.

According to Roberts, the cases most suitable for keratoplasty are conical cornea, small central opacities, and mild interstitial keratitis. The larger the opacity and the more extensive the preoperative corneal vascularization, the less chance there is for a clear graft.

PAUFIQUE discussed the indications for the therapeutic lamellar corneal graft.

He is of the opinion that the lamellar corneal graft, has three indications: optical, for superficial lesions occupying only a part of the corneal thickness; preparatory, in serious lesions of the cornea with dense, highly vascularized leucomas preparatory to a perforating graft; and therapeutic, for the treatment of progressive corneal diseases. The trophic action in keratoplasty is an interesting phenomenon.

Therapeutic lamellar grafting may be performed at the periphery or at the center of the cornea. This type of grafting is indicated in all forms of chronic or recurrent keratitis when all the usual treatments give no results, when the center of the cornea is in danger, or when a perforation of the cornea is imminent.

SHAFER presented the results of his experiments with homoplastic partial lamellar grafts on rabbits.

The experiments were performed to determine the effect of direct edge-to-edge suturing of partial lamellar grafts and to devise a method of overcoming the herniation of the recipient bed encountered in lamellar partial transplants.

Histologic sections were made after enucleations at 1 hour and 1, 2, 3, 4, 5, 7, 8, and 10 days postoperatively. It was found that no standard-sized graft persisted longer than the fifth postoperative day. The recipient bed was epithelialized at that time. All standard-sized grafts presented an epithelialized notch between the edges of the recipient and donor stroma. The notching was attributed to stretching of the recipient bed.

In a second series of partial lamellar corneal transplantations performed with the donor disc 1 mm. larger in diameter than the recipient bed, corneal sections were examined at 1, 3, 5, 7, and 10 days postoperatively. In spite of the oversize graft, a gap or notch was found in all sections but those which were made on the first and seventh postoperative days. Stretching and herniation of the recipient bed is not resisted by edge-to-edge corneal sutures. It is believed to occur during the operation before any retaining suture can be closed. Decompression procedures are suggested to prevent herniation of the recipient bed in lamellar corneal transplantations, at least in the soft cornea of the rabbit.

LAVAL discussed the pathology of removed corneal sections.

After the graft has been inserted, it becomes edematous during the first 24 hours and the epithelium is lost. The endothelium is always damaged to some extent, but part of it may remain on the graft. The majority of the stromal cells continue to live in the graft. There is no massive degeneration or replacement at any time during the postoperative course. The stromal cells are supplemented by newly formed keratoblasts from the cornea of the recipient. The epithelium is replaced by epithelium from the recipient cornea. The endothelium may be repaired from the uninjured cells of the graft or by cells from the recipient cornea. The wound is closed at first by a clot of fibrin followed by fibroblasts which form fibrous tissue between the graft and the adjacent cornea.

FREEMAN contributed his observations on embryonic corneal transplantation.

The study was organized to contrast the healing of embryonic corneal tissue transplanted to animals of the same and of different species.

He concluded that on transference embryonic corneal tissue grows moderately well, persists for several months, regresses, dies, and is finally replaced by the cells of the host.

KATZIN reported on the ultimate fate of the graft. If the cornea of the patient has a sufficient number of normal corneal cells in the graft bed, they may proliferate and enter the new structure and take over their function in it. When the cornea of the host is badly scarred so that only few normal cells are present the graft will not remain clear for more than a few weeks. When the cornea of the host is very much vascularized so that reparative processes proceed at a very rapid rate after transplantation, even though there may be many normal corneal cells in the bed, the graft becomes invaded by connective tissue and does not remain clear. In other words, the host's cornea gradually fills in with its own cellular elements while maintaining the original matrix.

BUSCHKE presented some of the dynamic aspects of tissue structure in corneal epithelium. Certain factors in determining success or failure in corneal surgery are related to the complex problems of viability of tissue, wound healing, and compatibility of the tissues.

The observed phenomena may be classified as degenerative, proliferative, and inflammatory. Buschke

presents many examples which demonstrate the possibility of modifying and directing by environmental agents the course of events which are casually related to the maintenance and re-establishment of functional and morphologic integrity of tissue, in prophylactic and therapeutic procedures.

LENZ discussed the value of radiotherapy for the prevention and obliteration of corneal vascularization. The result of the beta rays and low voltage roentgen rays to prevent or obliterate corneal vascularization is influenced chiefly by three factors:

1. The condition of the cornea at the time of irradiation and the preceding cause of opacification of the cornea. Best results are obtained if the opacity is caused by infection or degeneration of the cornea by traumatic ulcer. Corneal vascularization may be prevented or obliterated in about two-thirds of these cases and when due to other causes in about one-third of the cases. Prevention or obliteration of vessels by radiotherapy is as successful following keratectomy as keratoplasty, that is, in about 40 per cent of the cases.

2. The age of the capillaries. Because capillaries are endothelial cells they are sensitive to radiation. Postoperative prophylactic results are successful in 44 per cent of the cases; when visible vessels are present the incidence of success is only 33 per cent.

3. Dosage. Successful therapy with beta and roentgen rays depends upon adequate dosage. With beta rays this varied from 1,200 to 6,000 roentgens. With roentgen rays at 45 or 60 kv., the results were better when a dosage of over 600 roentgens was administered. (The average dose was from 1,000 to 5,000 roentgens per week). The most satisfactory distribution of radiation may be obtained by the use of beta rays, x-rays at 25 kv., or x-rays through a beryllium window with voltages from 30 to 100 kv. Nevertheless, 60 kv., no filters, 10 cm target skin distance has also given satisfactory results without the production of a cataract.

OKRAINETZ discussed beta irradiation of the eye with the radium-D applicator. This applicator is considered an effective source of beta irradiation for complementary treatment of benign lesions of the superficial structures of the eye. In no case of this series were the underlying or adjacent tissues injured.

PATON presented a number of illustrations of typical and of previously considered inoperable cases of typical corneal transplantation cases:

1. An amblyopic eye with completely scarred cornea, involving all the layers (no blood vessels). The penetrating corneal transplant has remained clear for 3 years. Although central vision was not improved there was considerable improvement in peripheral vision, as well as cosmetic improvement.

2. A conical cornea. Preoperative vision with correction was 20/300. Postoperative vision was 20/20 with a −5.0 D. sph−1.25 D. cyl.

3. Groenouw's dystrophia. Preoperative vision was 2/200. Postoperative vision was 20/30 with correction, following transplantation of a 6.0 mm. penetrating corneal graft.

4. Completely scarred cornea. Postoperative vision was light perception. Two previous 5.0-mm. transplants had been unsuccessful. Postoperative vision, 6 months after a 10-mm. corneal transplantation, was finger counting at 2 feet. The cosmetic improvement was marked.

5. Superficial central scar. Preoperative vision was 20/200. Vision after currettage and application of hydrochloric acid was 20/40.

6. Old keratitis (nonspecific in origin) after irradiation therapy for the destruction of small blood vessels. One year after a penetrating corneal transplant vision was 20/20.

7. Conical cornea after first corneal grafting operation. The graft became cloudy but no blood vessels were present. Vision with correction was 10/200. One year after the second grafting operation vision with correction is 20/30. The graft remained clear during 3 years of follow-up.

8. Adherent leucoma after beta irradiation to destroy several large vessels at the 6 o'clock position. Postoperatively there was marked cosmetic improvement.

9. Adherent leucoma. Optical iridectomy did not improve the condition. The cornea was clear 2 months after a penetrating corneal grafting operation.

TUDOR advocated his technique for corneal transplantation which involves the principle of cross sutures, slight shelving margins, the use of scissors, and the use of trephines of slightly different sizes. Cross sutures have, on the whole, been accepted. Concerning these cross sutures and the eight-point fixation, he emphasizes the importance of obtaining exact symmetry in the suturing.

VANNAS pointed out that he prefers the round graft and, contrary to the practice of other operators, he uses a mechanically driven trephine. With this high-speed trephine, he obtains a completely isolated transplant, not only from the donor but even from the recipient cornea in almost 10 per cent of the cases.

To keep the transplant in place he uses a very thin rubber membrane instead of sutures.

JOSHUA ZUKERMAN, M.D.

MOUTH

A Further Report on the Treatment of Micrognathia with Obstruction by a Plastic Procedure. Results Based on Reports from 21 Cities, 1948-1949. BEVERLY DOUGLAS. *Plastic & Reconstr. Surg.*, 1950, 5: 113.

The present article is a supplement to that which the author presented on the same subject in 1946 (*Plastic & Reconstr. Surg.*, vol. 1: 304).

Respiratory obstruction in cases of micrognathia is due to the tongue's falling backward and downward into the throat over the epiglottis in such a way as to act as a ball valve, which allows egress but prevents ingress of the air. The operation which the author proposed is designed to overcome this obstruction. A portion of the undersurface of the

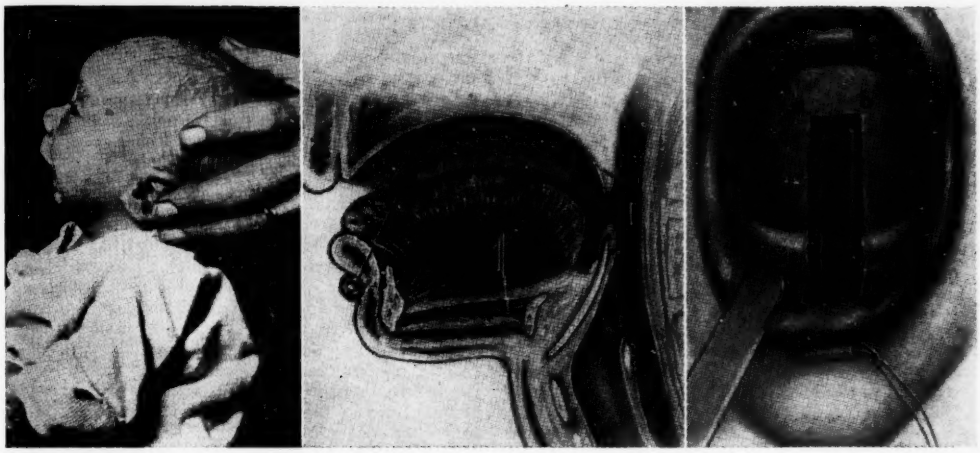


Fig. 1 (Douglas). a, Micrognathia patient. Note receding chin—"Andy Gump" deformity. Patient successfully treated by surgical fusion of tongue with lip. (Photo courtesy of Dr. Kenneth). b-c, Technique of surgical suspension or fusion of tongue to lower lip for relief of the inspiratory obstruction of micrognathia. b, Position of tension suture after excision of mucous membrane. Line ——position of suture; line....raw surfaces approximated; line------former position of tongue. c, Raw surfaces on tongue, gum, and lip approximated.

tongue and lip is denuded of mucous membrane as shown in Figure 1. The tongue is then held forward by suturing it to the lip and the respiratory difficulty is relieved. After 4 to 5 months, when the mandible has increased in size, the tongue can be released by a simple "Z" type of plastic operation.

The author believes he has obtained good results in 11 of his series of 12 patients.

Tabular reports, from questionnaires sent to plastic surgeons only, show 21 patients treated conservatively and 25 treated by the author's operation. Of the 21 only 35.7 per cent survived, a mortality rate of 64.3 per cent. JOHN J. BALLENGER, M.D.

Clinicostatistical Report on Carcinoma of the Mouth and Pharynx, Under Treatment from 1928 to 1945. General Formulations and Criteria of Evaluation. (Rendiconto clinico-statistico dei carcinomi della bocca e del faringe trattati dal 1928 al 1945. Impostazione generale e criteri di valutazione.) ALDO PERUSSIA. *Radiologia med.*, Milano, 1950, 36: 194.

The director of the Institute of Roentgenology of the University of Milano, Italy, had the material pertaining to the treatment by roentgen and radium therapy which had accumulated since the initiation of this Institute in 1928 subjected to a statistical study to serve as a sort of memorial for the work accomplished and to be used for comparison with results obtained elsewhere. Of course, much of this material has been reported previously; however, this is the first attempt at a comprehensive evaluation of all results procured in the nose and throat department in as far as the treatment of cancer by radiologic methods is concerned.

Different regions of the entire topographic area under consideration were entrusted to individual authors. Thus, the tumors of the oropharynx appear in the immediate future under the authorship of Perussia himself, those of the hypopharynx under Antoniassi, and those of the base of the tongue under Vecchi. In this preliminary communication some attempt is made to present such general principles of classification and of evaluation as will free the subsequent reports of a certain amount of repetition.

The inclusion in any of these tables of statistics implies that the condition is of malignant and of epithelial nature; however, cases in which no histological or other proof of such nature was available have nevertheless been included when such nature was suspected from the clinical course or the response to irradiation treatment. This has been done in order to avoid introducing a form of arbitrary selection in the work of classification. One of the major divergencies from the criteria selected by other authors in this field is found in the inclusion, among the carcinomas, of the carcinoma with cylindroid or adamantinoid aspects, and of the so-called lymphoepithelioma.

The duration of the tumor before treatment was instituted could at times be presumed only from anamnestic data; it will generally be understood to be the period of time between the first objective or subjective symptoms, reasonably imputable to the growth, and the initiation of treatment at the Institute.

With regard to the histologic type of the neoplasm, the author and his coworkers have in mind a complete revision of all available histologic slides

with the intention of attempting some revision of criteria which will permit of a more uniform classification of tissue findings; in the meantime they are limiting themselves to such differentiation as will establish as precisely as possible the cancerous or noncancerous character of the condition under study. Only three types of carcinoma are at present recognized histologically: (1) the spinocellular cancer, (2) the basocellular cancer, and (3) cancers which do not fit into the first two groups (basospinocellular, cylindromatoid, adamantinoid, and those with undifferentiated cells).

Macroscopic criteria are largely, of course, not suitable for statistical treatment; however, one of the variables which may be more or less exactly measured or enumerated is the primitive seat of the new growth; this can be realized in many cases only approximatively in so complicated and closely crowded an anatomical entity as the nose and throat. Of primal significance in this connection would naturally be the question of the unilateral or bilateral feature of the lesion.

Macroscopically, the size of the primitive growth is of especial importance, since in radium therapy, such as practiced at the Institute, the estimation of dosage is dependent upon the approximate determination of the dimensions of the growth to be treated. Here again the complex geometry of many regions of the nose and throat renders such determinations extremely difficult at times. At present all that is attempted is the estimation of the extension on the surface. The lesions are classified as to their approximate size into four groups. The first group consists of the lesions which measure up to about 4 sq. cm. on the surface (extremely circumscribed). The second group (circumscribed) measures approximately from 4 to 8 sq. cm. Finally, the third group measures more than 14 sq. cm.

The macroscopic critera of the so-called cytoarchitectonic comportment of the new growth result in the recognition of only 3 type forms. First, there is the predominantly vegetative type of growth tending to extend superficially. Second, there is the mixed form exhibiting nodular or irregular masses of exuberant superficial vegetations but the whole of it resting on an infiltrated base. Third is the case with rapid growth of the neoplastic tissues in depth and with scarce or absent exuberative overgrowth on the surface.

With reference to the determination of the presence or absence of metastases in the satellite lymph nodes, the condition may be merely suspected; that is, the gland is palpable, swollen, or is generally of such a character (column, form, consistency, location, eventual immobility, disposition) as would authorize the suspicion of its being the seat of neoplastic metastasis. This is the criterion of evaluation indicated by Ratti and generally followed by the author's group of workers.

Second, a hunt is made for any further possible evidence to substantiate the cited suspicion. If, for example, a previous operation has resulted in a histologic examination of a swollen gland in the suspected region and such examination was positive, this would, of course, be decisive; however, even if such examination was negative at the time, evidence will be sought in case of local recurrence or further involvement with the possible finding of a metastatic process secondary to the primary lesion.

Finally, such metastatic involvement of the satellite nodes is considered proved when the further clinical course has demonstrated the indubitable existence of such a condition, even though the subsequent treatment (irradiation therapy) has resulted later in the clinical healing of such a process.

In the further discussion of this material no attempt will be made to define particular regions of distribution of regional glandular metastasis other than the inframaxillary, submental, and jugulocarotid regions, and then one general category for the less frequently seen localizations. The question of unilateral or bilateral involvement is always, of course, of consummate importance.

The treatment of the primary growth has for many years consisted solely of irradiation in some form or other, the regional metastases being, as a rule, referred to the surgeon. During the earlier years the removal of the regional lymphatic tissues was followed by long periods of postoperative irradiation treatment; this has of late years been largely abandoned. When any surgical measures are used today on the primary lesion they nearly always take the form of superficial removal of the vegetative overgrowths with diathermy, that is, a "smoothing down" of the lesion. This applies only to growths which have received no treatment prior to arriving at the author's service or the services of his coworkers. When the patient arrives with a recurrent process the measures used are not standardized and may vary extensively from case to case.

The types of treatment used for the patients comprising this material have been the isolated or combined use of intratissue radium therapy, endocavitary radium therapy (frequently in the form of an endoral modelled apparatus), transcutaneous radium therapy, or radium treatment in the form of an externally modelled apparatus of Columbia paste, or, of late years, tele-Curie-therapy, ordinary roentgen therapy, and plesioroentgen therapy. For details of the techniques which have, through the years, become rather exactly standardized, the reader is referred to the textbook of roentgen and of radium therapy, written by the author's coworkers, F. Perussia and E. Pugno-Vanoni.

The criteria of cure have been essentially based on the classic 5 year period of survival; however, since this would cut out much of the latest and most interesting material, in some cases a separate estimation, based on a 3 year period of survival, has been added. When the patient has been lost to view, or when for other reasons the results, especially the final results, have had to be made on a presumptive basis, the most pessimistic view possible under the circumstances has been the rule.

The annual mortality for a given year (first, second, third years of survival, calculated from the period of the initiation of treatment) has been obtained from the following formula

$$Q=\frac{q}{q+I}$$

wherein: Q is the annual mortality (for a given year of observation);
q is the number of patients dying in that ear; and
I is the number of patients surviving at the end of that year.

It is evident that q+I represents the total number of patients exposed to the risk of dying during the year under consideration. This number, of course, gets progressively smaller, because of intercurrent and other deaths of the previous year and because a certain number of patients are lost to sight. The number of patients surviving at the end of any determined number of years from the initiation of treatment is obtained from the formula: $L_n=(1-Q_1)\ (1-Q_2).....(1-Q_n)$, wherein: $L_n=$ the survival figures at the end of the given year, and $Q_1, Q_2....., Q_n=$ the annual mortality for the first, second, ... given year from the period of initiation of treatment.

The percentage of survival may therefore be obtained by multiplying L_n by 100. If, finally, the estimation of the number of patients surviving at the end of a given year when compared with the total of cases under consideration that is, the "calculated" number of survivors for any given year, is desired, this can be obtained from the formula: $I_n=m\ L_n$, wherein: l_n equals the number of survivors "calculated" at the and of $_n$ years; m equals the total number of cases considered in the calculation (here it comprised also those cases which were followed up for a number of years inferior to $_n$).

It appeared advisable in the calculations with regard to determining the "calculated" number to include the cases which were eventually "dispersed," that is, those in which it has not been possible to obtain either evidence of survival or of death. For this the principle of the most pessimistic attitude, as previously explained, has been consistently applied. JOHN W. BRENNAN, M.D.

NECK

The Symptomatology and Clinical Forms of Cancer of the Larynx (Sintomatología y formas clínicas del cáncer de la laringe). JUSTO M. ALONSO. *Rev. otorrinolar.*, 1949, 9: 103.

The subjective symptoms observed in laryngeal cancer reveal a disturbance of respiration, phonation, and deglutition: sensitive or reflex disturbances, pain, cough, hemorrhages, bad breath, swelling of the lymph nodes, and signs of intoxication and general debility which appear in an advanced stage of the disease. It is important to inquire into the familial history of the patient. Although he does not believe in the heredity and contagion of cancer, the author has observed repeatedly that there are families in which cancer abounds and attacks more than one member in the same localization. The antecedents of the patient deserve careful examination and must include previous diseases, especially syphilis and tuberculosis; previous presence of other cancerous localization, of cutaneous hyperkeratosis, and of leucoplakias; general habits such as the use of tobacco, especially if excessive, and of alcohol, especially if of bad quality; work in places where there are irritating dusts or vapors; and unsanitary and badly ventilated living quarters. The age and sex of the patient are important since in 95 per cent of the author's cases the laryngeal cancer occurred in males, the majority of whom were between the ages of 45 and 65.

Laryngeal cancer is found to be increasing in part because of more accurate diagnosis but also because of an actual increase in its incidence. Success in its treatment depends on early diagnosis. Therefore, the author analyzes the five principal localizations of the disease and the characteristic symptoms observed.

1. Cancer of the glottis in which the principal sign, and the only one for several months and sometimes for years, is a variable but permanent hoarseness in a healthy looking subject, which will evolute toward a secondary picture of asphyxia.

2. Perilaryngeal cancer in which the disturbances are more of pharyngeal nature, interfering with deglutition; later there is rather rapid general decline, local pain, and pain radiating toward the ear, fetid breath, adenopathy, and, still later, asphyxia, with relatively conserved voice, and in any case less involved voice than in the preceding type.

3. Cancer of the epiglottis and arytenoepiglottic folds in which the disturbances are minimal in the beginning and do not produce disorders of phonation, alimentation, and respiration. In its evolution, it causes adenopathy which is mistaken for the primary lesion, pain in the ear or odynophagia, or it spreads toward the entrance to the esophagus with resulting dysphagia. Later it may cause dysphonia and especially dyspnea by invasion, fixation, or edema of the endolarynx.

4. Cancer of the vestibule in which the symptoms in the beginning are minimal, consisting of slight discomfort in the hyoid region which may be taken for the annoyance of a chronic tonsillitis and which increases to produce asphyxia and adenopathy without disturbances of deglutition and generally without fetid breath, but with late pains.

5. Cancer of the subglottis in which the symptomatology is treacherous and deceptive, beginning with paroxysmal attacks of asphyxia which later become permanent; the change in the voice is inconstant and atypical. This type will often cause asphyxia before the cancer is diagnosed, but it can be recognized by careful examination and interpretation. RICHARD KEMEL, M.D.

The Surgical Treatment of Laryngeal Cancer (Tratamiento quirúrgico del cáncer laríngeo). JUSTO M. ALONSO. *Rev. otorrinolar.*, 1949, 9: 122.

The author recalls that the invariable line of conduct of the surgeon in the presence of laryngeal cancer must be (1) to save the life of the patient, (2) to preserve, if possible, the functions of the organ, and (3) to palliate the sufferings of the patient if cure is impossible. There are three interventions which may be called classical and which in a more or less broad concept are used by the majority of the surgeons: extirpation of a vocal cord by laryngofissure, extirpation of the epiglottis by pharyngotomy, and total laryngectomy.

For the past 10 or 12 years, and after having used during 23 years all the varieties of classical techniques, Alonso has tried to systematize the operations suitable for the extirpation of tumors that do not invade the vocal cords and therefore preserve the integrity of the glottis, which is the most important part of the larynx. He discusses the personal techniques which he uses for the three principal types of tumors. In tumors of the pyriform sinus he applies the method which he has called "vertical partial laryngectomy," in which he recommends that a lateral pharyngeal stoma always be left and closed plastically 1.5 to 2 months after the primary intervention. For tumors of the vestibule he has devised the "horizontal partial laryngectomy" which allows the preservation of phonation. It is based principally on the histologically proved fact that the tumors of the base of the epiglottis and of the ventricular bands (which always behave in the same manner) never spread downward and thus leave the vocal cords intact except only for involvement by inflammatory edema. Finally, in subglottic tumors he uses an "anterior partial trachectomy." He recommends this technique for cases of benign anterior subglottic tumors which cannot be removed by the natural passages, and for anterior cancers which are not much developed and do not reach the commissure of the vocal cords or the vocal cords themselves.

Consequently, the indications for this technique are few and up until now the author has been able to use it in only 1 case, a benign tumor which extended over the internal anterior border of the trachea from slightly below the anterior commissure of the vocal cords to the space between the second and third tracheal rings. The patient was operated upon 1 year ago and has kept his normal voice.

RICHARD KEMEL, M.D.

SURGERY OF THE NERVOUS SYSTEM

BRAIN AND ITS COVERINGS; CRANIAL NERVES

Tumors of the Thalamus (Tumeurs du thalamus). CH. PAPAIOANOU and R. HOUDART. *Sem. hôp. Paris*, 1950, 26: 555.

Tumors of the thalamus are relatively rare and represent about 1.5 per cent of all intracranial tumors. They may be observed at any age, but show a predilection for subjects under 30. They are mostly gliomas. The authors report 13 cases, 7 of which were verified at autopsy; in the other 5, the patients left the hospital or autopsy was refused, but there can hardly be any doubt about the site of the tumor. Six patients were between 10 and 20 years of age and 8 were between 11 and 26 years. In 8 cases there were 3 glioblastomas, 2 astrocytomas, 1 astroblastoma, 1 astroblastoastrocytoma, and 1 metastasis; the other 5 cases seem to have included 2 tubercles and at least 1 glioma.

The outstanding feature is the extreme lack of similarity between the cases, the only clinical element common to all being intracranial hypertension. The symptomatology of these tumors is particularly polymorphic and varied. Some symptoms belong to the classic syndrome described by Déjerine and Roussy for the vascular lesions; others, although usually occurring in vascular lesions, are explained by the physiology of the thalamus, for example, mental disturbances; still others are due to repercussion in the vicinity by the tumor itself or by the edema which surrounds the tumor. However, none of these different symptoms are pathognomonic or constant. In some cases there may be a particularly rich syndrome with diffuse motor, superficial, and deep sensitive, visual, mental, and sympathetic disturbances, while in other cases the syndrome may be so quiet that, if it were not for the presence of intracranial hypertension, it would pass completely unrecognized. Thus, if in the first case the clinical diagnosis may be suspected, there is nothing in the second case to allow thinking of the thalamus, and ventriculography will be indispensable to make the diagnosis.

To read the films correctly it must be remembered that the thalamus forms the posterior part of the lateral wall of the third ventricle, so that a tumor strictly limited to the thalamus leaves the anterior part of the third ventricle intact; the thalamus also forms the middle part of the floor of the lateral ventricle, so that a tumor here will obstruct the passage of the cerebrospinal fluid and cause upstream dilatation of the ventricular system.

Removal of these tumors constitutes an intervention of extreme gravity, and even simple exploration was fatal in 5 cases. Therefore, when the tumor manifests itself only by signs of intracranial hypertension, it is best to be satisfied with the operation of Torkildsen for derivation of the cerebrospinal fluid, followed by roentgen therapy.

RICHARD KEMEL, M.D.

Neurosurgery in Young Children. HAROLD C. VORIS. *Arch. Surg.*, 1950, 60: 906.

The author discusses the special problems that may arise in infants with regard to anatomy and physiology of the nervous system, and some of the pathologic problems that may be encountered.

Stress is laid upon the importance of proper understanding of the preoperative and postoperative care in surgery directed towards infants under 2 years of age. The discussion includes descriptions of the usual congenital deformities, such as spina bifida, cranium bifidum, intracranial hydrocephalus, Arnold-Chiari malformation, and some mention is made of the surgical treatment which has been undertaken in these various conditions.

Chronic subdural hematoma and brain abscess are also mentioned, as well as intracranial tumors which are often relatively malignant when appearing in the first 2 years of life.

Stress is placed upon immediate, adequate replacement of blood and body fluids that are lost during surgery in infants, and the particular attention that must be paid to body temperature and the maintenance of adequate fluid intake in the postoperative state.

Tables of development with regard to weight, head and chest circumference, and brain weights, as well as a table of general development in infants up to 2 years are included. HOWARD A. BROWN, M.D.

SYMPATHETIC NERVES

The Late Results of Sympathetic Surgery for Arteritis of the Lower Extremities (Les résultats éloignés de la Chirurgie Sympathique dans les artérites des membres inférieurs). P. DECOULX, P. GAUTIER, and G. NICODÈME. *Lille chir.*, 1949, 4: 157.

The authors discuss in a detailed report the surgical indications, treatment, and results of arteritis of the lower extremities based upon a study of 117 cases. Arteritis is a progressive disease leading to amputation; the condition of the patient may be improved and sometimes stabilized by proper surgical intervention. The disease may be divided into three stages: in the early stage ischemia of the lower extremity is secondary to exertion and is characterized by intermittent claudication; the second stage is characterized by severe pain when the legs are kept in horizontal position and by relief of pain when they assume a vertical position; and in the third stage the pain is constant and severe and the limb may become gangrenous.

Three types of operative procedures are considered by the authors in the treatment of arteritis.

They are always preceded by percutaneous arteriographic or aortographic studies which visualize the degree, the nature, and the site of the vascular obstruction, and the state of the collateral circulation. Arteriectomy of the obliterated portion of the vessel is thought to increase the collateral circulation, to stop abnormal reflexes, and to prevent central extension of the thrombus. This operation was usually performed in old patients but gave little help when gangrene was already present in the extremity. Isolated femoral arteriectomy gave good results in 32 per cent of the operative cases. Lumbar sympathectomy was found to produce a temporary vasodilatation and to suppress possible ganglionic reflexes. Removal of the sympathetic chain with the first and second ganglia was considered preferable to a lower lumbar sympathectomy because it resulted in a preganglionic sympathectomy for the entire lower extremity. This procedure did not always relieve intermittent claudication; it often stopped pain and prevented high amputation in cases of existing gangrene. It was thought to be of little value when the collateral circulation was poor or when the obliteration involved most of the peripheral segment of the vessel. Lumbar sympathectomy was followed by good results in 57 per cent of the cases. Lumbar sympathectomy associated with arteriectomy yielded good results in 70 per cent of the cases and was considered the operation of choice. In obliteration of the popliteal artery, lumbar sympathectomy was found to be the best procedure, while in obliteration of the iliac artery, arteriectomy and lumbar sympathectomy gave good results in 42 per cent of 12 cases.

Adrenalectomy was considered to be of value only in early cases; it was performed in 11 cases and gave only 3 good results. It was thought to reduce sympathetic hypertonus and thus to prevent the occurrence of vascular spasms. It was advocated for the treatment of thromboangiitis obliterans.

The authors report favorable results in 52 per cent of the 117 patients and poor results, including 12 deaths, in 48 per cent of the patients. Good results were obtained in 64 per cent of the cases in the first stage of the disease, in 54 per cent in the second stage, and in 33 per cent in the third stage. The indications for these conservative operations were localized arterial obliteration, satisfactory collateral circulation, and good circulation within the main arterial trunk below the site of obstruction. Conservative treatment was contraindicated and amputation was necessary when gangrene was progressive, in patients beyond the age of 70, and when there was loss of circulation within the artery distal to its obstruction.

GEORGE PERRET, M.D.

Sympathectomy in Hypertension. ROBERT PLATT and S. W. STANBURY. *Lancet*, Lond., 1950, 1: 651.

The authors present the results of operation for hypertension in 80 patients, some of whom have been followed up for 2 or 3 years.

In the majority of cases, the results generally are considered to be poor, and the authors are very critical of the good results reported by several American authors. It is stated that the reason for these unusually good results is due to three factors: (1) insufficient control, with failure to observe the blood pressure for a long enough time before operation was performed; (2) failure to appreciate the great variability of blood pressure in benign hypertension; and (3) ignorance of the natural history of benign essential hypertension, with lack of appreciation of its relatively good prognosis in the majority of the milder cases.

They rather generally condemn the operation by stating that the majority of cases of essential hypertension are either too mild to warrant operation or too severe, too old, or too arteriosclerotic to benefit from it. It is finally admitted that there may be a small middle group in which sympathectomy will, even judged by the stricter standards, produce real, apparent, and significant benefit.

The results as outlined here are based chiefly upon a reduction in the diastolic pressure in the recumbent position. It is admitted that subjective improvement may occur without a material drop in blood pressure, but such cases are not considered "successful" by the authors.

The majority of patients selected for operation in this series had diastolic pressures of 130 mm. of mercury or more when the patient was ambulant, which tended to be at least 120 mm. when the patient was at rest in bed.

Three types of operations were employed: the so-called Smithwick dorsal lumbar operation, the Adson subdiaphragmatic splanchnic resection with removal of the first, second and third lumbar ganglia, and the Boyd operation done in three or four stages with bilateral removal from the fourth dorsal to the fifth lumbar ganglia. A fourth procedure, called the Adson plus, included a subdiaphragmatic splanchnic resection and lumbar ganglionectomy, and unilateral resection supradiaphragmatically from the fourth to twelfth dorsal ganglia.

In only 11 of the 80 patients was a significant and lasting reduction of blood pressure achieved. Most of these patients were young women under 40 years of age, suffering either from essential hypertension or from renal hypertension with good renal function.

Comment is made with regard to the postural tachycardia and dyspnea seen in the more extensive Boyd operation, but no final conclusions were drawn as to the advantage of any one of the operative procedures over and above the other.

A final comment states that sympathectomy should very rarely be advised in hypertensive disease.

The choice of patients in this series again has included chiefly those with severe hypertension and a poor prognosis, which would account for the relatively unfavorable results, and is in accord with other reports in the English literature.

HOWARD A. BROWN, M.D.

SURGERY OF THE THORAX

CHEST WALL AND BREAST

Giant Mammary Myxoma.. Report of a Case in a Young Woman with Rapidly Enlarging Fibroadenomas in the Contralateral Breast. EDGAR P. MANNIX, JR., and AUGUST F. WILDNAUER, JR. *Brooklyn Hosp. J.*, 1949, 7: 139.

Johannes Mueller, in 1838, first described giant mammary myxoma of the breast under the name "cystosarcoma phyllodes." Since then, well over 100 cases have been described under at least thirty different names. The lesion is believed to be a benign variant of fibroadenoma, and is the result of tremendous enlargement of a pre-existing fibroadenoma of the intracanalicular type. It is most frequent in the fifth and sixth decades. The diagnosis can usually be made from the history and physical findings of (1) long duration followed by rapid growth, (2) absence of nipple or skin involvement, (3) large size, and (4) terminal ulceration from mechanical factors.

Treatment is simple mastectomy. Malignant changes are rare; when they occur, regional nodes are seldom involved, dissemination usually being hematogenous.

An unusual case is reported of a very large giant myxoma (4785 gm.) in the left breast of a 29 year old woman, which progressively enlarged to ulceration over an 8 year period, and was treated by simple mastectomy with later axillary dissection. The lymph nodes were uninvolved. A right simple mastectomy was also done because of multiple fibroadenomas. FRANK B. QUEEN, M.D.

TRACHEA, LUNGS, AND PLEURA

One Hundred and Fifty Interventions (Pulmonary Exeresis) for Tuberculosis (A propos de 150 interventions d'exérèse pulmonaire pour tuberculose). M. BÉRARD. *Mem. Acad. chir.*, Par., 1950, 76: 147.

The indications for operation in this series of patients with tuberculosis were bronchial stenosis in 40 cases, a destroyed lung in 39, a subthoracoplasty residual cavern in 23, a subextrapleural residual cavern in 17, a cavern of the lower lobe in 12, a giant cavern of the upper lobe in 5, and purulent tuberculous pleurisy in 14. No matter what the indication may be, it is necessary that the other lung is not only uninvolved but also possesses a satisfactory functional value, that the general condition and the organic defenses of the patient are sufficient, that no other tuberculous foci are present, and that the lesions have been stabilized as much as possible by the antibiotics. Lobectomy or pneumonectomy will be best supported by young subjects and becomes a matter of chance after the age of 40.

The operative risk is very small. There were 5 operative deaths (3.3 per cent): 2 from anoxemia, 2 from very early hemorrhage, and 1 from gaseous embolism. There were 5 deaths in the immediate postoperative period: 4 from contralateral tuberculous evolution between the sixth and fifteenth days, and 1 from respiratory insufficiency of a presumably healthy lung on the fifth day. Thus, the total operative mortality amounts to 6.6 per cent. Unfortunately, there is a risk of secondary complications.

One of the patients during the follow-up developed a fatal contralateral tuberculous evolution; this was a borderline case before the intervention. Thus, it would seem that this risk is practically negligible, considering that some patients were followed-up for more than 2 years. On the other hand, more or less early respiratory insufficiency, with dyspnea, cyanosis, and than a sudden dramatic crisis of acute pulmonary edema has sometimes been observed and has caused 3 deaths, respectively, 1 month, 6 weeks, and 4 months after the operation.

The worst and most frequent complications are secondary empyema and bronchial fistula. Secondary empyema may be insidious or appear suddenly after the formation of a bronchial fistula; it was observed in 35 patients. A distinction must be made between pure empyema without bronchial fistula, and empyema complicated by fistula: the first is often healed by thoracoplasty, while the second has an extremely grave prognosis. Bronchial fistula in most cases occurs late and is a pathologic condition that cannot be charged to the technique of bronchial suture. In 2 patients it was observed before the fifteenth postoperative day. In 15 patients it appeared after the third week and often much later, even in the seventh month in 1 case. These fistulas are due to tuberculization of the stump or to the development of a small tuberculous empyema in contact with the bronchial suture. They have resulted in 17 deaths. Consequently, the total mortality of the series has been slightly over 20 per cent. This figure may seem to be high.

In reality, operation has been performed in many patients with enormous, copiously secreting lesions which were highly evolutive and could not be stabilized by the antibiotics. These heroic indications were nevertheless justified since, in addition to the inevitable failures, there have been a number of unhoped-for successes. RICHARD KEMEL, M.D.

Considerations with Reference to the Surgical Treatment of the Bronchiectases. Anatomopathologic Study (Considérations à propos du traitement chirurgical des bronchectasies. Etude anatomopathologique). A. DUPREZ. *Acta chir. belg.*, 1949, 48: 659.

Thirty resections of lung tissue were performed on 29 patients with bronchiectasis since the end of 1946 at the Saint-Pierre Hospital in Brussels, Belgium.

The author, together with collaborators and under the direction of A. Deloyers, has already reported on the clinical findings and results of surgery. In this article he discusses the anatomopathologic aspects of the same material.

A new method was developed for studying the precise form and extent of the pathologic changes present in pulmonary tissue removed at operation. This consisted in insufflating and hardening the tissue, and then the air passages were filled with a plastic and the tissues subsequently digested away with hydrochloric acid. The plastic moulages thus secured then served as models for macroscopic study.

By this method two basic types of bronchiectatic cavity were distinguished. The first type is designated as the preterminal bronchiectatic cavity; this seems to correspond to the older designation of cylindrical cavity. The dilatation is cylindrical; lies in the midst of aerated, often seemingly normal, pulmonary tissue; is not of large size; and contains the apertures of ingress of the bronchioles in its walls. The other type is the so-called terminal, or sacular, cavity which is a large cystic dilatation lying in atelectatic, infected, lung tissue and is devoid of any trace of bronchiolar apertures.

The two types described are the basic ones; however, the author has been able to demonstrate all forms of transition between the two and has even been able to find a still more advanced form in which the lobe has become completely atelectatic with huge saccular cavities of which the walls have come in contact and broken down, thus producing huge intercommunicating tracts which enclose in the mesh thus formed the branches of the pulmonary artery and vein.

In the specimens in which the pulmonary arteries and veins were injected simultaneously with the bronchi, the intense congestive manifestations of the atelectatic lung tissue were striking and demonstrated the nature of the short-circuiting of the blood circulation through the airless atelectatic tissues.

On the whole, the author thinks that on examination of these preparations it would be indeed difficult not to conclude that all these various forms of bronchiectatic manifestation are merely a part of one progressive process, and that this conclusion carries with itself the postulation that in the presence of bronchiectatic lesions, even presenting the most perfectly benign appearance, the indication for pulmonary exeresis is present. Even the small preterminal lesions lying in the midst of aerated lung tissue offer the indication for removal while the operation is still easy to accomplish, before the advanced changes, which render dissection difficult and hazardous and reduce the resistance of the patient, have developed.

JOHN W. BRENNAN, M.D.

Simple Excision of Lung Abscess. CRANSTON W. HOLMAN. *Surgery*, 1950, 27: 546.

Because of the divergence from the accepted method of pulmonary resection in the treatment of abscess of the lung, Holman reports a case of lung abscess which was treated by excision. The excision was surprisingly easy and the maximum amount of lung tissue was conserved. Three cases exemplifying the details of the procedure are reported. The prerequisites given for successful excision are:

1. A single abscess in which lobectomy would sacrifice too much normal lung tissue.

2. The infecting organisms should be reasonably sensitive to antibiotics in order to prevent overwhelming postoperative sepsis and toxicity.

3. A degree of chronicity is desirable to insure both a minimum surrounding pneumonitis and an adequate capsular demarcation of the abscess from the normal lung.

4. The importance of covering the bronchial stump, no matter how small, with either a pleural flap or a free pleural graft cannot be overemphasized. This provides for the trapping of blood and plasma about the bronchial stump, which facilitates the normal process of wound healing.

5. The same precautions should be observed as when any type of lung resection is performed; that is, expert anesthesia, careful dissection, adequate blood replacement, and attentive postoperative care with the use of antibiotics and chemotherapy.

STEPHEN A. ZIEMAN, M.D.

Bronchial Adenomas. Clinicoradiologic Study and Description of 6 Observations (Adenomas bronquiales, Estudio Clinicorradiológico y relato de 6 observaciones). MARIO M. J. BREA, FRANCISCO AGUILAR, and ANDRÉS A. SANTAS. *Prensa méd., argent.*, 1950, 37: 412.

Brea *et al* describe a series of 6 cases of bronchial adenomas. In 4 of them the tumor was resected, by pneumonectomy in 3 and lobectomy in 1, and the other 2 were subjected to endoscopic resection. All of the patients survived and at the time of this report they were all in good health.

The article is well illustrated and extensively reviews the Argentine as well as the universal literature on the subject. WILLIAM E. RICKETTS, M.D.

Clinical Polymorphism of Primary Carcinoma of the Bronchi (Le polymorphisme clinique du cancer primitif des bronches). M. CHEVALIER and P. GALLUS. *Bruxelles méd.*, 1950, 30: 641.

Eight bronchial cancers have been observed during the past year at the Civil Hospital at Etterbeek, Belgium (near Brussels), in which the diagnostic possibilities contrasted sharply with the abundant literature devoted to the special techniques for the early recognition of this affection. The cases are reported in some detail for the purpose of showing that in such instances the chief emphasis in diagnosis must be placed upon a study of the clinical symptoms.

In the first case, that of a 54 year old male, there had been attacks of bronchial cough each winter for many years. In this last winter, however, the attack had resembled a bronchopneumonia and the

roentgen examination showed a consolidation of the right middle lobe of the lung. The patient complained most bitterly of pain in the lumbar region where nothing could be uncovered. Bronchoscopy disclosed an evidently abnormal right middle lobe bronchus; however, neither tubercle bacilli nor cancer cells could be determined. Penicillin therapy did not bring the relief to be expected in simple bronchopneumonia. Autopsy disclosed a small cell cancer of the diseased bronchus. The tumor had infiltrated the lower half of the right lung and there were metastases in the mediastinum and liver.

In the second case, that of a 50 year old male, the symptoms and roentgenologic findings were those of lung abscess; again treatment did not give satisfactory results. The abscess cavities were multiple and of oddly irregular conformation. They filled with lipiodol, which is rather unusual for tuberculous cavities. Again no tubercle bacilli and no cancer cells could be demonstrated. In this patient, just as in the first described, autopsy uncovered a carcinoma of the lower branch of the left bronchus which had broken down to form abscesses. There were metastases in the spleen, suprarenal glands, and liver, which were symptomless except for a mild terminal icterus.

In the third case, that of a 65 year old male, the symptoms and roentgenologic findings were those of mediastinal tumor; however, the left lower lobe of the lung suggested atelectasis. This was the only sign which raised the suspicion that the tumor might be a parahilar bronchial carcinoma with predominantly mediastinal and distant metastatic development. Autopsy confirmed the suspicion.

In the fourth case reported, that of a 53 year old male, the findings were those of a tuberculous pleurisy of the base of the right lung. Without apparently remembering that tuberculous pleurisy is rather rare in a man of 53 years, and without any exhaustive search for other etiologic factors (as roentgen examination following aspiration of the pleural effusion should have disclosed the tumor mass), the physician sent the patient to Switzerland. Autopsy disclosed an adenocarcinoma involving the lower half of the right lung with metastases to the pleura, pericardium, and suprarenal glands.

In the fifth case, that of a 58 year old male with chronic bronchitis since 1914 and diabetes since 1945, the symptoms were those of pain such as occurs in neuralgia of the cervicobrachial plexus on the right side, and later of cough, expectoration, and febrile attacks. Roentgenography at this time uncovered an atelectaticlike appearing condensation of the right pulmonary apex and a rounded mediastinal mass at the level of the aortic arch. Bronchoscopy showed an abnormal aperture of the right upper branch of the bronchus; however, biopsy was negative for carcinoma. In this patient there was no autopsy, but the probable diagnosis was cancer of the bronchioles of the right upper lobe.

These 5 case reports are, in the authors' opinion, sufficient to illustrate the diversity of manifestations which may be presented by bronchial carcinoma and the importance of a clinical diagnosis based on elimination of the other possible pulmonary affections. JOHN W. BRENNAN, M.D.

The Early Diagnosis of Bronchial Carcinoma (Zur Fruehdiagnose des Bronchuskarzinoms). F. SPATH. *Wien. med. Wschr.*, 1950, 100: 188.

In some clinics the frequency of bronchial carcinoma in men now exceeds that of carcinoma of the stomach. The heretofore pessimistic attitude toward the disease should be abandoned in view of its frequency, the possibility of early diagnosis without particular difficulty, and the fact that it can be cured surgically with a relatively low operative mortality. In order to achieve early diagnosis one must not overlook or minimize the first symptoms and signs, which are often not severe. Every suspicious complaint must be investigated and clarified because the seriousness of the symptoms is often concealed by the apparent good general condition of these patients until late in the course of the disease.

In more than half the cases a dry cough is the first symptom of bronchial irritation. Next in importance is the occurrence of a striking "strange or uncomfortable feeling" which gradually increases to pain. The pain in the beginning is caused by atelectasis and is aggravated by deep inspiration. Later, pain results from involvement of the pleura, chest wall, nerve roots and plexus, and the vertebral column. A mucoid or purulent sputum, occasionally blood-streaked, is a further suspicious symptom. Gross hemoptysis is rare. Increased temperature, which is the rule in tuberculosis, is lacking. In 9 per cent of cases the initial signs are those of an intrathoracic infection, while 50 per cent of the later cases show pneumonia, lung abscess, pleuritis, or empyema. Some patients have a heavy, labored respiration bordering on dyspnea as the first sign. The doctor is likely to think of grippe, a cold, tuberculosis, or of atypical pneumonia. Any of these signs are suspicious of bronchial carcinoma and demand thorough clinical investigation.

In early cases physical examination may only serve to heighten suspicion of the disease so that other methods of study must be added. It is important, however, to palpate the supraclavicular and axillary nodes and the liver. Roentgen examination of the lung fields is of most value in suspected cases, or as a routine measure in the susceptible age group. If roentgen examination is negative in a suspected case, further study should be carried out immediately and not after one or more intervals, since the average patient presents himself 8 or 9 months after the onset of symptoms. As the next procedure serial laminagraphs should be made. These will demonstrate the branches of the pulmonary tree without the use of contrast media, and their value lies not in demonstrating the tumor itself but rather the bronchial contours which may show distortion, narrowing, or occlusion. Through the use of bronchography with the aid of instillation

of a contrast medium, displacements, narrowing, or filling defects may be demonstrated. In the case of carcinoma near the hilus, contrast visualization of the esophagus and esophagoscopy should not be neglected. For central tumors direct visualization and biopsy by means of the bronchoscope can be carried out. Certain signs of inoperability may be determined by means of the bronchoscope. Further diagnostic procedures are cellular diagnosis of sputum specimens or saline washings or of pleural fluid, pneumothorax and thoracoscopy, and biopsy of lymph nodes. Puncture biopsy of peripheral tumors and probably sealed over pleural fissures is not recommended. Exploratory thoracotomy is necessary for diagnosis in a small percentage of cases and is often the only means of determining the operability. Exploration is advisable in almost every case in which the history and examination provide a suspicion of bronchial carcinoma.

JOHN L. LINDQUIST, M.D.

Mechanical Forces in the Chest and Thoracoplastic Operations (Meccanica statica del torace e toracoplastica). FELICE PARODI. *J. internat. chir. thorax.*, 1949, 1:235.

An attempt was made, on a model of the human chest, to reproduce the mechanical factors encountered by thoracic surgeons in the plastic procedures on the ribs with a view to obliterating the cavities occurring within the pulmonary tissues in pathologic conditions. The model consisted of an anatomical preparation of the human thoracic skeleton which was set up on a base so as to conform to the normal erect posture of the individual when breathing. Various ligaments and muscles were represented by graduated steel springs, rubber bands, and rigid wires arranged in such a manner as to reproduce exactly the various forces and checks of the human thorax in respiration.

The lung tissue itself was represented by a radiating system of cords, each attached to a dynamometer and extending from the theoretical center of elasticity and weight of the lung in a radial direction to the various corresponding points on the ribs. These dynamometers were graduated to represent the various lines of potential retraction (load) of the lung. The weight of the lung on each side was represented by a weight suspended from the center (600 gm. for the right lung, 400 gm. for the left). On the model the various forces were measured during respiratory movements (produced automatically) and following various thoracic plastic procedures.

The thoracic operations consisted of 5 plastic procedures: (1) excision of the first rib, (2) anterior partial thoracoplasty, (3) posterior partial thoracoplasty, (4) anterolateral partial thoracoplasty, and (5) lateroposterior partial thoracoplasty. These interruptions of the costal continuity were all done in the classic manner.

Since the retractile potential of the lung is an expression of the weight of the lung itself, the relationships of the different ribs may be expressed as the parts of the weight of the lung which each carries. By this method it was found that the upper ribs carry the greater part of the weight of the lung. The weight borne, or load, decreases from the upper to the lower ribs, the greater part being borne by the posterior segments of the rib. Thus, any operation which removes the posterior support of the lung weight (posterior thoracoplasty) and which involves the upper ribs will drop the center of gravity lower and will be more effective than the anterior or lateral thoracoplasty in obliterating any cavities that are present, especially in the upper regions of the lung.

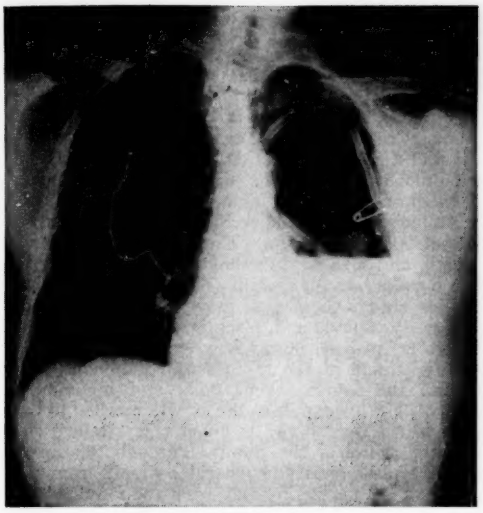
The mobility of the mediastinum (represented in the model by an elastic septum) is least back near the spinal column (for posterior thoracoplasty) and up under the sternum (for anterior thoracoplasty). Thus, with the former operation the lung tends to collapse anteriorly with slight lateral (toward the opposite lung) displacement; with the latter operation (anterior thoracoplasty) the collapse is backward and somewhat lateral. With the laterally placed thoracoplasty the lung collapses inward; however, this collapse is inward but it is rendered less effective by the yielding of the mediastinum toward the opposite side of the chest. Thus, the superficially located cavities are effectively collapsed by the laterally placed thoracoplasties while those placed deeply near the hilus are less amenable to the procedure. Of course, the effective collapse of the cavities placed low down near the diaphragm, where the load carried by the individual rib is much less, is harder to obtain by thoracoplasty and here other methods (exeresis of the phrenic nerve) may come under consideration.

The author does not change the indications already established by thoracic surgeons but merely tries to place such indications on a more objective basis. It is his opinion that the surgeon, before attempting a thoracoplastic operation, should give careful consideration to the principles of mechanical loading of the thoracic bony cage. The lesion to be attacked should be located carefully in the lung by means of anteroposterior and lateral stratigraphic roentgenography and the operation should be planned from the information thus procured.

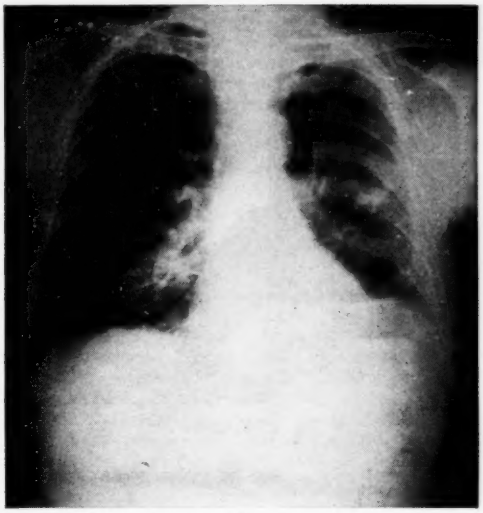
JOHN W. BRENNAN, M.D.

Streptococcal Enzymatic Débridement. WILLIAM S. TILLETT, SOL SHERRY, L. R. CHRISTENSEN, ALAN J. JOHNSON, and GEORGE HAZLEHURST. *Ann. Surg.*, 1950, 131: 12.

It has been demonstrated recently that concentrates obtained from cultures of hemolytic streptococci contain streptokinase (streptococcal fibrinolysin) and streptodornase (streptococcal desoxyribose nuclease). The mixture of these two concentrates in saline can be injected into areas of the body where there are collections of fibrinous or purulent exudates, to assist in their dissolution or their removal. The categories in which this is clinically useful are: (1) loculated, postpneumonectomy hemothorax; (2) traumatic hemothorax; (3) sterile locu-



a



b

Fig. 1 (Tillett *et al.*). Traumatic hemothorax. a. Tube below level of fluid but drainage ineffective. Complete collapse of lung present. b. Roentgen ray taken at time of discharge from hospital, 55 days after treatment started.

lated empyema; (4) bacterial empyema; (5) local infections such as osteomyelitis and paranasal sinusitis; and (6) miscellaneous chronic ulcerative lesions.

Illustrative histories of cases in the above categories are given. The usual history is that of a thick, loculated exudate which proved impossible to remove by aspiration. Following the instillation of a mixture of the two streptococcal enzymes, the fluid became thinner and could be readily aspirated. In the instance of osteomyelitis, a chronic draining sinus became smaller and its exudate became thinner and less malodorous after the enzymatic débridement. In one patient with a postpneumonectomy empyema, the offending organism was Bacillus pyocyaneus. This failed to respond to instillations of penicillin, sulfadiazine, streptomycin, parachlorophenol, or urethane. After numerous injections of the enzymatic mixture, the infection subsided completely. It is believed that following removal of the débris and exudate present in the pleural cavity by the streptococcal enzymes, the natural antibacterial factors of the host were capable of destroying the pyocyaneus organisms. This could not be accomplished by antibiotics and other bactericidal agents as long as the exudate and débris were present.

The authors conclude that in patients in whom the presence of extravascular clotted or loculated hemorrhage without infection is the chief difficulty, the rapid lysis of fibrin and its associated coagulum may be accomplished by streptokinase. This obviates the probable necessity of surgical decortication in posttraumatic hemothorax and similar conditions. When infection has occurred the mechanical effects of loculation are complicated by the coating of the tissue surfaces with the desoxyribose nucleoprotein of purulent exudates, and streptodornase is more applicable.

The use of this mixture of streptococcal enzymes to eradicate the loculations or exudations of chronic infection has been referred to as "streptococcal enzymatic débridement." The following changes are noted when effective action has occurred: thinning of the exudate, outpouring of viable leucocytes, decrease in the number of, or disappearance of, the locally infecting bacteria, subsequent decrease or disappearance of exudate, and rapid regrowth of tissues and epithelium. Additional studies regarding "streptococcal enzymatic débridement" are now in progress. C. Frederick Kittle, M.D.

ESOPHAGUS AND MEDIASTINUM

Surgery of the Thoracic Esophagus (Cirugia del esofago toracico). Ignacio González G. *Arch. Soc. cirujan.*, Chile, 1949, 1: 17.

Surgery of the thoracic portion of the esophagus has grown to its present status because of the perfection of the anesthesia, better understanding of the biological principles, and improvements in the preoperative and postoperative care.

Pneumothorax, injury of the mediastinum, complicated anatomic conditions, operative shock, and technical difficulties in suturing are no longer considered obstacles to surgery of the esophagus.

The author treated surgically 5 patients with carcinoma of the esophagus and 1 patient with benign

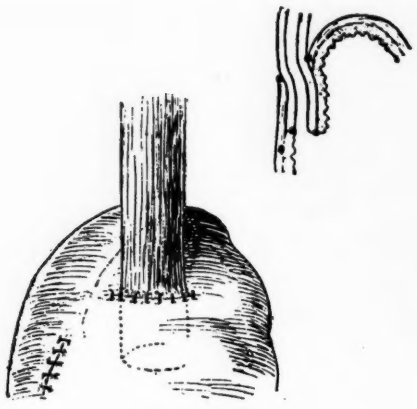


Fig. 1 (González).

stenosis probably caused by circumscribed chronic esophagitis. One patient with cancer succumbed to right pneumothorax and hemothorax, which aggravated his poor general condition. The 5 other patients recovered.

If the oral or parenteral route of feeding fails to attain a satisfactory nutritional level, jejunostomy may be required for the purpose of alimentation before the radical operation is undertaken.

The author employs the left transpleural approach and re-establishes the esophagogastric continuity after incision of the diaphragm. He stresses the necessity of excision of the lymph glands located in the hilum region, along the aorta and the esophagus, in the subdiaphragmatic region, and along the lesser curvature of the stomach. If the right pleura is inadvertently injured, it is advisable to finish the dissection of the tumor before the tear is sutured, as this improves the exposure. To make the esophagogastrostomy more secure, the author forms a subserous tunnel in the stomach wall through which the proximal end of the sectioned esophagus is introduced (Fig. 1).

After the operation, negative pressure is maintained in the left pleural cavity by means of water-sealed suction. JOSEPH K. NARAT, M.D.

Posterior Mediastinal Goiter (Les goitres du médiastin postérieur). ÉRIC NÈGRE and ANTONIN BALMÈS. *J. chir.*, Par., 1950, 66: 190.

A case of posterior mediastinal thyroid is reported. This raises the number of reported cases to 16. Thirteen of these were on the right side, while in 3 the exact location was not specified.

The case here reported was that of a 37 year old woman who had been suffering for a year with violent attacks of coughing. She had been treated for 6 months for whooping cough. Roentgenographic examination disclosed the presence of a large mass with sharply delimited contours in the upper part of the right hemithorax. The trachea was evidently deviated to the left. The tumor extended from the second rib behind to the sixth. The projection in profile demonstrated the integrity of the anterior mediastinum and of the retrosternal space. The mass did not follow the movements of deglutition. Roentgenographic examination after the creation of a pneumothorax on the right side excluded a pulmonary tumor. The diagnosis was neurinoma of the posterior mediastinum.

An incision was made vertically in the right interscapulovertebral space. The arcs of the third, fourth, and fifth ribs, in the area corresponding to the incision, were resected. Through this incision, leaving always the pleural cavity intact, the tumor was easily exposed and, after ligation of its superior (vascular) pedicle, it was removed from its bed on the right side of the trachea and esophagus and behind the superior vena cava and innominate artery. The lower pole of the growth reached to the hilus of the right lung; its upper pole attained the superior orifice of the thorax. Through this aperture the mass received a vascular supply from the region of the neck (probably from the inferior thyroid artery). This vascular pedicle passed behind the right subclavian artery.

The removed tumor was 8 by 7 cm. in size, encapsulated, and permeated with large sinuous veins. The surface of a cross section presented the aspect of a colloid goiter. The vesicles of this growth presented histologically an extremely active proliferation of the lining epithelium. Many of the vesicles were small (microcysts) with a rather diluted colloid content. At other places the vesicles were poorly differentiated and, in fact, were frequently represented by solid cords of atypical thyroid cells resembling a trabecular adenoma. There were no atypical nuclei or abnormal mitotic figures. The histologic diagnosis was microcystic vesicular thyroid adenoma.

The authors accept the theory of Lahey as to the route of downgrowth of this tumor toward the anterior mediastinum (substernal thyroid) except that the tumor of the mediastinum passes behind the subclavian artery and to the right of the trachea and esophagus between the large vessels of the ascending aorta in front and the vena cava superior and crossbranch of the vena azygos behind. This position is regarded by the authors as corresponding rather to the midmediastinum than to the posterior portion of this structure.

The treatment is, of course, definitively surgical, and for this there are only two routes available. The first route is that followed in this patient and the one usually chosen for the neurinoma of this area. The second route is that through the pleural cavity and is preferable for very large growths.

The 16 case reports here mentioned therefore constitute the establishment of the identity of a new form of tumor manifestation. However, the authors believe that with the progress of surgery of the mediastinum this tumor will be ascertained to be

much more common than is here suggested. The ratio of the sexes thus far involved has been 13 women to 3 men. The authors do not believe that this tumor was a development of aberrant thyroid tissue in the region involved, but that it represented a true downgrowth from the thyroid in the neck, perhaps from the isthmus region and perhaps caused to grow downward first by the muscular contractions of the act of deglutition and later by the suction effects of respiration. JOHN W. BRENNAN, M.D.

MISCELLANEOUS

Funnel Chest and Allied Deformities of the Thoracic Cage. CHARLES W. LESTER. *J. Thorac. Surg.*, 1950, 19: 507.

Funnel chest is a symmetrical or asymmetrical funnel-shaped deformity of the chest wall produced by a short central tendon of the diaphragm. The character of the deformity is determined by the portion of the central tendon which is shortest. A short midportion of the tendon causes retraction of the xiphoid and lower sternum with a resultant drawing backward of both single and fused costal cartilages to a symmetrical funnel. Shortening of one or both lateral leaves of the diaphragm exerts pull directly on the costal arch and may result in a transverse grooving across the anterior chest wall below the xiphoid. The maximum depression of the chest wall is on the side of greatest shortening of the tendon.

The funnel sternum is accompanied by a secondary exaggeration of the dorsal spinal curve and an increase in the downward slant of the ribs so that the individual has round shoulders and a long narrow chest with a decrease in its anterior-posterior and lateral diameters. The cosmetic deformity is considerable, and increases with growth of the child.

Although the lung may be distorted and compressed to a 25 per cent reduction in volume, exertional dyspnea is attributed to interference with cardiac dilatation.

Operative correction is indicated for moderate to severe impairment of exercise tolerance and to prevent irreversible bony deformity in young children. The psychological aspects are emphasized.

The operative procedure used on infants up to 16 months of age includes resection of the apex of the costal arch to detach the xiphoid from the sternum. The substernal ligament, a prolongation of the linea alba on the posterior surface of the sternum, and some diaphragmatic attachments to the arch are severed.

A more radical operation is necessary in the older age group. The costal cartilages below the second, and including those of the costal, arch are resected subperichondrially as far laterally as the point where the backward curve begins, and far enough to include the lower border of any existing transverse groove. The xiphoid is detached from the sternum. A transverse wedge osteotomy of the anterior table of the third sternal segment is made so that the sternum may be fractured and elevated by stainless steel wires passed through drilled holes in its lower end. Traction is obtained by fastening the wires to an external appliance placed transversely across the chest. This is left in place about 2 weeks.

Results of the simple operation in 2 patients operated upon at about the age of 1 year have been good, but in 8 other somewhat older patients the results were equivocal. The authors reserve this operation for very young children with severe deformity and pressure symptoms. Best results were obtained with the radical operation on patients between the ages of 2½ to 4½ years, but operation at any age will afford relief of pressure symptoms and about 80 per cent correction of the deformity. There have been no purulent infections and no deaths among the 31 patients operated upon.

THOMAS LANE STOKES, M.D.

SURGERY OF THE ABDOMEN

ABDOMINAL WALL AND PERITONEUM

Disruption of Abdominal Wounds. WILLIAM I. WOLFF. *Ann. Surg.*, 1950, 131: 534.

The author presents a series of 1700 consecutive laparotomies in which the incidence of wound disruption was 2.6 per cent. Comparisons were made from the standpoint of the patient's age and race, the presence of cancer, the type and location of the incision, the suture material, and the method of closure.

Of the systemic factors concerned in wound healing, age, hypoproteinemia, and, to a lesser extent, race, seemed to influence the frequency of dehiscence. The season of the year, vitamin C deficiency, anemia, and sensitivity to catgut could not be indicted as significant determinants in this series. While wound separation in the cancer patient was common, cancer could not be divorced from age and other factors as a predisposing condition.

The type and the location of the incision did not seem to affect the disruption rate materially, except for the McBurney type of incision which afforded a high degree of protection. Placing a viscus in the incision definitely increased the risk, while drains did not. In several cases, disruption occurred in spite of retention sutures.

The most essential single aspect in the prevention of wound disruption is the intimate approximation of peritoneal layers, so as to prevent the entrance of an omental wedge.

Postoperative complications, particularly coughing and vomiting with their subsequent great increase in intra-abdominal pressure, are important factors in the production of dehiscence, and intensive efforts should be directed at their prevention and control.

Treatment may be either conservative with the use of tamponade and strapping, or operative. No one type of closure appears superior to another. The mortality rate in this series was 11.1 per cent. Follow-up showed a significant incidence of incisional hernias, regardless of the method of management.

ELY ELLIOTT LAZARUS, M.D.

Spontaneous Hematoma of the Abdominal Rectus Muscles (L'ematoma spontaneo dei muscoli retti addominali). ITALO FLORIO. *Gior. ital. chir.*, 1949, 5: 775.

The author reports 2 cases of spontaneous hematoma of the abdominal rectus muscles which represent the two extreme forms of the disorder. The first occurred in an arteriosclerotic and hypertensive woman of 74, who had carried to term 6 pregnancies and had recently contracted bronchitis with obstinate coughing, during which she noted the sudden appearance of a slightly painful abdominal swelling. The second case occurred in a woman of 56, who had had 1 pregnancy, and for the past few days a cough and slight fever; about 1 hour before admission she felt a strong tearing pain in the hypogastrium during an attack of coughing, and a few minutes later she had vertigo with a sensation of falling, and she had to lie down.

The history of the first patient revealed several factors predisposing to the disorder: when young, she had had typhoid which causes degenerative phenomena in the fibers of the abdominal recti with resulting marked decrease of their resistance; pluriparity, which has the same damaging effect on the vitality of the abdominal muscles; arteriosclerosis, which alters the structure of the vessels and decreases the blood supply; and hypertension, which has a continuous traumatic action on the vascular walls. The flaccidity of the abdominal wall due to the scarcity of fat and to the senile hypotonicity of the muscles made it easy to demonstrate that the swelling was parietal. Roentgen examination, which was made for the sake of complete study rather than of diagnostic necessity, gave no significant information and suggested more a disorder of the abdominal cavity than of the abdominal wall. The diagnosis was easy and was based on the history, the objective findings, and exploratory puncture. At operation the hematoma was found to be intramuscular and encapsulated; there were no bleeding vessels and it was thought that the hematoma was due to partial muscular rupture. An effort was made to approximate the thick, sclerotic walls of the cavity; a rubber drain was left in and discharged a small amount of serosanguineous fluid for 3 days.

In the second case the general symptoms were those of shock or of acute and severe internal hemorrhage. The exclusion of rupture of extrauterine pregnancy, the absence of antecedents which would suggest the existence of one of the diseases that might result in hemoperitoneum, and the impression that the swelling in the region of the left rectus muscle was not intra-abdominal led to the diagnosis of spontaneous hematoma of the rectus; a lesion of the left epigastric artery was suspected. At operation through a left paramedian incision, a large hematoma, mostly preperitoneal, and rupture of the inferior epigastric artery were found. The hematoma was emptied, the artery ligated, and the wound closed in layers without drainage. RICHARD KEMEL, M.D.

Peritoneal Recessus and Foramen Formations and Associated Intra-Abdominal Hernia and Strangulations. HANNES SAURAMO and JUHA TAPIOVAARA. *Ann. chir. gyn. fenn.*, 1950, Supp. 2.

The material studied included 100 fetuses and 100 adults examined soon after death. All material studied was macroscopically normal. This study was supplemented by a compilation of all surgical cases of intra-abdominal hernia and foramen strangu-

lation treated in Finland for the period from 1934 to 1947. There were 637 cases, which shows that such cases are less rare than is generally believed.

Detailed study of the peritoneum was started about the middle of the nineteenth century and about the same time surgical descriptions of intra-abdominal hernias with incarceration were mentioned in the literature. There is a marked variation in nomenclature and descriptions of these hernias. Later writers, as the present authors, have attempted to standardize and clarify the nomenclature and descriptions.

The authors describe five recesses in the duodenojejunal region and determined their incidence. Most common is the (1) recessus duodenomesocolicus cranialis which lies to the left of the cranial end of the ascending duodenum. It is present in 39 per cent of the fetuses and 32 per cent of adult subjects. The recessus duodenomesocolicus caudalis (2), which is closely related to the recessus duodenomesocolicus cranialis, and may actually share a common opening into the peritoneal cavity, was present in 35 per cent of the fetuses and 32 per cent of the adults.

The recessus parajejunalis (3), a pouchlike formation cranial to the first part of the jejunum, was present in 4 per cent of the adults. The fetal incidence was not given.

The recessus paraduodenalis (4), a pouch-shaped formation lying beside the most caudal part of the duodenum occurred in 2 per cent of the subjects.

The recessus retroduodenalis (5) lies adjacent to the junction between the caudal and ascending duodenum, opens in the caudal direction, and extends behind the duodenum. It occurred in a single case in an adult, among the specimens examined.

The recessus intermesocolicus transversus, which was not found, is a formation lying about the middle of the transverse mesocolon; it opens downward and extends toward the omental bursa.

Internal herniation in the duodenojejunal region in the surgical cases was found in 4 cases, of which 3 were fatal. The authors find it hard to correlate the pouches found anatomically with the description, or lack of description, of herniations found during surgery in this region. They suggest that perhaps the cause of the herniations is to be found in variations in the rotation of the intestine rather than in the small recess formations.

Three recesses and 1 fossa were described in the cecal region. The recessus iliocecalis cranialis opening to the left is superior to the terminal ileum and to the left of the ascending colon. It occurred in 72 per cent of the fetuses and 40 per cent of the adults.

The recessus ileocecalis caudalis is a pouchlike formation limited by the terminal part of the ileum, the cecum, and the vermiform appendix. It usually opens caudomedially. It was found in 49 per cent of the fetuses and 49 per cent of the adults.

The retrocecal recess is a pouchlike formation situated dorsad to the cecum and limited by the parietocecal folds; it opens downward, and partial mobility of the cecum is essential to its presence. Retrocecal recess was found in 5 per cent of the fetuses, and fossa cecalis (less pronounced than the recess) in 16 per cent; in adults retrocecal recess was present in 16 per cent and fossa cecalis in 27 per cent.

Only 3 cases of ileocecal hernia occurred in the surgical cases studied.

The incidence of recesses in the region of the colon in fetuses and adults was: (1) recessus paracolicus dexter (lateral to the ascending colon) 5 and 21 per cent, respectively; (2) recessus paracolicus sinister (lateral to the descending colon) 16 and 16 per cent, respectively; and (3) recessus intersigmoideus, 24 and 52 per cent, respectively. The first two recesses are of little clinical importance or interest. Herniation into the intersigmoid recess is reported but rarely. Its presence is conditioned by accompanying fixation anomalies of the intestine.

Studies were made of the epiploic formation in all specimens. The foramen was uniformly present; it led to the omental bursa, and its size varied within normal range.

A chapter is devoted to the description of rare recessus formations encountered in the specimens. The most important occurred in the ileocecal region, particularly in relation to a Jackson's membrane.

In the abdominal cavity, abnormal foramina may be present in the mesotenon, mesocolon, and greater omentum. Strangulations of bowel are reported throughout all of these foramina. Only 1 case occurred in the examined specimens, and that in the mesotenon in the ileocecal region in a fetus.

Based on this report, the common and typical recessus formations are the duodenomesocolic, the pericecal, and the intersigmoid. From the surgical cases enumerated it is evident that the common and typical hernias are the mesentericoparietal and the pericecal. The relation of the surgical mesentericoparietal hernia and the anatomical duodenomesocolic recessus could not be clarified by the authors.

The incidence of different peritoneal formations is remarkably high. Their presence alone, however, does not suffice to give rise to surgical complications. The following essential factors must be present: (1) the recess must be sufficiently large and have a small mouth; (2) the foramen must be large enough, and (3) the intestine or greater omentum must be mobile.

FREDERICK C. HOEBEL, M.D.

The Significance of Relaxed Inguinal Rings. L. KRAEER FERGUSON and MARK W. WOLCOTT. *Ann. Surg.*, 1950, 131: 584.

There are marked differences of opinion as to the significance of relaxed subcutaneous inguinal rings. Four thousand health records of a large university for the years 1937 to 1939 inclusive were examined. There were 392 relaxed subcutaneous rings among the 4,000 men examined. This group and a similar control group were then contacted by letter and asked if they had or had not undergone a hernia repair. Fourteen persons with relaxed rings developed a hernia over a period of 9 to 11 years from the date of the original examination. In the same

period the control group (those not having relaxed rings) had 8 hernia operations. This difference is not considered statistically significant.

F. J. LESEMANN, JR., M.D.

GASTROINTESTINAL TRACT

Transthoracic Gastrectomy in a Case of Cancer of the Cardia (Transtorakalne wyciecie żoladka w przypadku raka wpustu). JÓZEF DRYJSKI. *Polski przegl. chir.*, 1949, 21: 986.

A 53 year old woman entered the Holy Ghost Hospital in Warsaw, Poland, suffering from pains in the pit of the stomach and left epigastrium, loss of appetite and weight, a sense of pressure in the stomach, "rotten egg" belching, and weakness. The test for occult blood in the stool was positive and the roentgen examination afforded the typical findings of a large cancer of the stomach located high up toward the cardia.

At operation the eighth rib was resected, the left pleural cavity opened, and the diaphragm incised, under intratracheal closed-circuit anesthesia (pentothal, nitrogen monoxide, curare). The fist-sized tumor was found to have spread over the left half of the lesser curvature of the stomach. The gastrectomy was started by an incision through the gastric wall on the greater curvature near the esophageal attachment and carried around the tumor area, emerging on the lesser curvature. The tumor was thus removed, including the lesser omentum and its lymph glands, and a long roomy tube consisting of the half of the stomach on the side of the greater curvature was left. This tube was closed with two rows of sutures (catgut plus silk) and the stump of the esophagus, which was quite short, was implanted into the gastric cupula. The histologic diagnosis was carcinoma solidum.

During the operation the patient was given blood and 5 per cent glucose in physiologic salt solution; this treatment was continued at intervals during the postoperative period. At operation a fine stomach tube had been inserted as far as the duodenum and was left in place for 5 days; through this tube the patient was given milk and tea at intervals. After the tube was withdrawn fluids were swallowed without difficulty.

Penicillin and the sulfonamides were used in the usual manner at the time of operation, and when a pleural effusion occurred on the left side on the eighth postoperative day the fluid was aspirated and a solution of penicillin injected in replacement.

Three months later the patient was able to leave the hospital in excellent condition. Healing was complete. Eight months after operation the patient writes that she is perfectly well, has gained in weight and strength, and can walk several kilometers at a time.

The advantages of the transthoracic approach to cancer of the cardia are, in the author's opinion, the wide exposure of the involved area, the ability to do the esophagogastrostomy under direct control of the eye, and, finally, the power to extend the excision operation to cases which previously could not be so treated. The author agrees with Lahey (Lahey, F. H., and Marshall, S. F. *Surg. Gyn. Obst.*, 1941, 73: 341) that the method can be extended to include total gastrectomies, with perhaps the inclusion of a splenectomy. JOHN W. BRENNAN, M.D.

Deforming Antritis Secondary to Ulcer of the Angle of the Lesser Curvature (L'antrite déformante secondaire à l'ulcere de l'angle de la petite courbure). F. WARMOES. *Acta gastroenter. belg.*, 1950, 13: 19.

Warmoes recalls that in 1938 he reported a number of these antral deformities of various degrees and mentioned sclerosis of the lesser curvature, inflammatory swelling of the mucosa and of the entire antral wall, and perivisceritis as being the responsible anatomopathologic factors; in 1945 he added pyloric hypertrophy. In addition to these organic factors, there is also a functional factor which plays a large part in the production of the roentgen picture of this secondary antritis. Since the functional influence varies greatly according to cases, there is a great variety of forms of secondary antritis designated by such terms as absent, flattened, very small, triangular, conical, sugarloaf, and tunnel-like antrums. The conical deformities seem to be more frequent than the tunnel-like changes. Sclerosis of the lesser curvature plays an important part in the aspect of the antrum in some cases; it causes deviation of the antrum.

Many pathologists have described pyloric hypertrophy in antritides as secondary, or not, to ulcer of the angle of the lesser curvature, but roentgen reports of pyloric hypertrophy in ulcer patients were rare before 1945. Warmoes must have seen about 40 cases of pyloric hypertrophy which were secondary to ulcer of the angle, but only 3 without ulcer: these 3 cases were operated upon and found to be gastritis, but in 2 of them the question arose whether they were not healed ulcer cases. Thus, according to his experience, pyloric hypertrophy of adults, the so-called hypertrophic pyloric stenosis of adults, is nearly always a complication of ulcer; he does not believe that pyloric hypertrophy is secondary to spasm of the pylorus but that it is an inflammatory reaction. The muscular hypertrophy is not always limited to the pylorus; it may continue into the musculature of the antrum and produce a picture of elongated cone or of a sugarloaf.

Warmoes does not believe that the fibromuscular atresia, and particularly the secondary pyloric hypertrophy, must lead to stenosis. His roentgenograms show a rigid pylorus, but it is always open; the absence of pyloric spasm and the frequency of pyloric sclerosis explain this. In antritis with pyloric hypertrophy, the violent peristalsis of pyloric stenosis is always absent. He believes that the gastric stasis often seen in ulcer of the angle of the lesser curvature is nearly always due to gastric atony which is typical of this ulcer. For instance, in 7 of 9 cases of secondary pyloric hypertrophy operated upon, he observed

normal or nearly normal evacuation of the barium meal; the other 2 cases presented stasis which did not seem to be caused by stenosis but by atony of the stomach.

In most cases deforming antritis is a sign of ulcer of the angle of the lesser curvature. There is nearly always a niche: it may be very small and is often on the posterior aspect of the lesser curvature; it is absent when the ulcer heals. A typical ulcer history in the presence of antral atresia makes it almost certain that there is an ulcer of the angle of the lesser curvature even if the roentgenograms show no niche, for ulcer can never be excluded without gastroscopy. Atresia of the antrum in itself is not an indication for operation, since the patient does not suffer from it when the ulcerous period has passed and the atresia usually does not lead to stenosis. The evolution of the ulcer must indicate the treatment.

RICHARD KEMEL, M.D.

On the Performance of the Billroth II Resection in Gastroduodenal Ulcer (Zur Ausfuehrung der Resektion nach Billroth II beim Magen-Zwoelffingerdarmgeschwuer). F. HOLLENBACH. *Chirurg.*, 1950, 21: 26.

This study is based on 1,148 severe cases of gastroduodenal ulcer in which the author deviated from the usual technique of the Billroth II resection in that he did not use clamps nor suture the mucosa, and used catgut instead of silk for the anastomosis. Results amply justified these changes in technique since the mortality rate in this series was much lower than that mentioned in any large series of the literature. In addition, follow-up examinations revealed excellent results in 90 per cent of the cases and not a single recurrence of ulcer.

In the first 2 decades of gastric surgery, carcinoma only was operated upon and, when ulcer was later also treated surgically, the experience gained from the former was applied to the latter, although there are basic differences between the two diseases. While the anacid gastric contents of carcinoma are highly infectious, the acid gastric ulcer must be regarded as aseptic. Therefore, and also because the fasting stomach is empty and can be emptied by lavage in gastric stenosis, the use of clamps in ulcer operation is superfluous. In more than 2,000 gastric resections for ulcer done without clamps, no damage has ever resulted from spilling of the gastric contents. The use of clamps also offers disadvantages which may result in marked injury to the patient.

The use of clamps causes an artificial ischemia, and the surgeon tries to make sure of hemostasis with a continuous mucosal suture which, however, does not allow visual verification of the hemostasis as the clamps can be removed only after completion of the suture of the posterior and anterior walls. Hollenbach prefers to obtain hemostasis by individual ligation of the vessels. Other disadvantages of the continuous mucosal suture are the creation of a space between this suture line and the row of Lembert sutures, and the resulting undesirable and dangerous phenomena occurring in this space.

As to the use of silk or catgut, the silk sutures do not heal into the wound but are eliminated after a certain period which may be as long as a year. In some cases the sutures are not eliminated and fistulas form about the threads which hang inside of the stomach. In the depth of the suture line, foreign body granulomas originate about silk threads or their remnants and keep the anastomosis in a condition of chronic inflammation. Anastomotic ulcers with silk threads or silk coils visible in the bottom of the ulcer have been described by many authors. But even without recurrent ulcer, these fistulas and granulomas may cause a chronic inflammation and swelling of the anastomosis which must be considered in connection with the postoperative gastrojejunitis and as a partial phenomenon of the latter. The exclusive use of catgut is therefore imperative. In 400 resections in which catgut sutures were used, there has been no suture insufficiency, and the mortality rate of 1.5 per cent has been the lowest hitherto reported in the literature, although the series included not only primary but also secondary operations for jejunal peptic ulcer, perforation, and acute hemorrhage in about 30 per cent; the mortality rate for primary resections was 1.25 per cent.

The author performs a posterior gastroenterostomy and passes only the efferent jejunal loop through the opening in the mesocolon; this passage must always lie to the left of the duodenal flexure to avoid angulation of the loop. This operation has the advantage of being applicable in all cases. So-called gastric atony and bleeding from the anastomosis have not been observed, and postoperative vomiting has been rare; only about 10 per cent of the patients have eliminated some bloody mucus on the first or second day. There have been 2 duodenal insufficiencies, although only a Finsterer exclusion resection had been carried out.

The mortality in 1,146 resections, including 61 secondary operations, was 25, or 2.2 per cent; in 1,085 primary resections it was 21, or 1.9 per cent. The causes of death were abdominal in 11 cases and extra-abdominal in 14. RICHARD KEMEL, M.D.

Uncommon Findings in Gastroduodenal Oncology: Lipoma (Reperti non comuni di oncologia gastroduodenale: i lipomi). ODOARDO LINOLI. *Arch. ital. mal. app. diger.*, 1950, 16: 85.

The autopsy of a man, aged 73 years, disclosed among other findings a fungating, papilliferous carcinoma of the pyloric antrum and, adjoining it, a subserous, suppurating lipoma on the anterior wall of the stomach.

The postmortem findings in a man, aged 46 years, revealed a submucous lipoma on the posterior wall of the second portion of the duodenum, 1 cm. from Vater's papilla.

The author collected from the literature 59 cases of gastric lipomas and 20 cases of lipoma of the duodenum. Lipomas of the stomach occur mostly

in men of adult or senile age; they are usually single, have a globular or oval shape, are found most frequently in the pyloric region, and rarely cause an ulceration of the overlying mucosa.

Duodenal lipomas occur with equal frequency in both sexes, in adult or old persons, are rarely multiple, have an oval or round shape, and seldom cause an ulceration of the overlying mucosa.

Subserous lipomas of the stomach or the duodenum are rarities as compared with submucous lipomas.

The rare occurrence of lipomas of the duodenum may be ascribed to the generic antiblastic constitution of this organ, as evidenced by the low frequency of other tumors in this region.

JOSEPH K. NARAT, M.D.

Notice on a Modification of the Finney Operation. Section of the Pyloric Sphincter Followed by Gastroduodenal Anastomosis (Note sur une modification apportée a l'opération de Finney. Section du sphincter pylorique suivie d'anastomose gastro-duodénale). A. FOLLIASSON and H. GREPINET. *Rev. chir.*, Par., 1950, 169: 122.

The author had excellent results with his modification of the Finney operation in 2 conditions: (a) periduodenitis accompanied by achalasia and not improved by prolonged medical treatment, and (b) small ulcers of the anterior aspect of the first portion of the duodenum.

Different techniques of gastroduodenostomy are discussed in this article. Mere section of the pyloric sphincter often proves unsatisfactory as the pyloric ring may be restored and lead to recurrence of the contraction and spasms.

The author suggests a method which combines the advantages of the Judd and the Finney operations. The incision should be right paramedian and transrectal rather than supraumbilical to give better access to the duodenum. The superior flexure and the second portion of the duodenum should be mobilized by lowering the root of the transverse mesocolon at its attachment to the duodenum. This method permits anterior rotation of the duodenum without incurring the danger of tension and assures sufficient length of the anastomosis which should reach distally to the level of the ampulla of Vater. The second portion of the duodenum is anastomosed to the prepyloric antrum.

The operation avoids the disadvantages of the "antiphysiologic" classical gastroenterostomy.

WERNER M. SOLMITZ, M.D.

Critical Study of Péan's Type of Gastroduodenal Anastomosis After Gastrectomy, and of the Treatment of Its Sequelae (Étude critique de l'anastomose gastro-duodénale type Péan après gastrectomie du traitement de ses séquelles). COSTANTINI and PIÉTRI.

Péan's gastroduodenal anastomosis, also called Billroth I operation, preserves the anatomic and physiologic conditions better than other methods, and is not followed by the dumping syndrome. A further advantage of this operation lies in the fact that all maneuvers are performed above the mesocolon within a relatively limited cavity and without submesocolic manipulations. The operation requires less time than competitive procedures.

The blood vessels of the duodenum must remain intact, the cuff must be sufficiently long, and its walls must not be damaged, and, if the stump of the stomach cannot be brought down without tension, the duodenum must be mobilized.

The authors performed Péan's operation on 10 patients. In 2, a painful syndrome developed after the operation.

Factors responsible for complications after gastroduodenostomy may be divided into 3 groups: (1) anatomic, (2) physiologic, and (3) mechanical.

The first group is responsible for the majority of complications. Under the influence of curare no difficulty may be experienced in approximating the gastric stump and the duodenum, but considerable traction may be exerted by the stump later on. Moreover, the blood supply to the first portion of the duodenum is frequently unsatisfactory, so that ischemia may lead to a secondary necrosis. Finally, the relatively narrow stoma may cause a retention of food and a postoperative inflammatory stenosis, edema and, finally, a stricture.

As to the physiologic factors, the mucosa of the duodenal bulb may be the site of reflexes which stimulate acid secretion in the same manner as the antrum. Vascular factors probably also are partially responsible for the greater frequency of peptic ulcers after gastroduodenostomy than after other methods of anastomosis. Poor blood supply favors production of an ulcer.

Mechanical factors militate strongly against gastroduodenostomy. After the anastomosis the duodenum is subjected to traction to the left. This fact has not yet received due attention in the literature although the traction may be responsible for early as well as late complications. Postoperative duodenal atony, probably caused by section of the vagi nerves, permits the duodenum to be pulled to the left to a certain extent, but lack of elasticity and also the sclerotic infiltration of its walls facilitate relaxation of the suture line, with the resulting danger of a fistula or peritonitis. A kinking of the third portion of the duodenum may also be provoked by the traction. The latter also explains the painful postoperative syndrome without an ulcer. The normal acute angle of the first portion becomes obtuse after the operation. The elongation of the duodenum, caused by traction, may produce a festooning effect. Duodenal stasis may result. The surgeon has at his disposal two alternatives: to secure the freedom of anastomosis, he does not resect a sufficiently large portion of the stomach, or by executing the gastrectomy properly, he impairs the mobility of the anastomosis.

The treatment of late complications, be it stricture, peptic ulcer, or dilatation of the right portion of the

duodenum, is always surgical and consists of taking down the anastomosis, closing the duodenum, and performing Polya's gastrojejunostomy.

JOSEPH K. NARAT, M.D.

Massive Gastrointestinal Hemorrhage Due to Jejunal Diverticula. DONALD D. KOZOLL, JOHN A. MCMAHON, and JAMES P. KIELY. *J. Am. M. Ass.*, 1950, 142: 1258.

The authors report a case of massive hemorrhage due to jejunal diverticula, the seventh of its kind in the literature.

The patient was a 64 year old white male who continued to bleed in spite of excellent conservative management in the hospital. A preoperative diagnosis of bleeding ulcer was made and laparotomy was performed with the idea of doing a gastric resection. At laparotomy no bleeding point could be found, although jejunal diverticula were noted. The bowel was pink and appeared not to contain blood. Because of the lack of awareness that jejunal diverticula could cause massive gastrointestinal bleeding, it was decided to conclude the operation. The patient continued to bleed postoperatively until his condition became critical. It was then decided that further surgical intervention was mandatory and a plan was proposed to resect the segment of jejunum involved by diverticula and to check the specimen as a source of bleeding. If it did not prove to be the source of hemorrhage, then a gastric resection would be undertaken on empiric grounds.

After adequate preparation the patient was operated upon a second time, and 51 cm. of jejunum were resected with a primary anastomosis of the proximal jejunum to the ileum. When the specimen was opened it was found that about one-half of at least a dozen diverticula contained 2 to 10 mm. mucosal ulcerations and several of them were filled with clotted blood. The surgeons then felt confident enough that the source of bleeding was eradicated and closure of the wound was immediately effected. The patient made an uneventful recovery except for two small residual tarry stools.

The diverticula reported are of the acquired type occurring along the mesenteric border at a point where the intestinal wall is weakened by perforating blood vessels. It is interesting that 16,600 c.c. of tarry stool were measured in this case. If this amount had not been collected it is certain that the patient's degree of hemorrhage would have been underestimated. The patient belonged to blood group O and was Rh negative. In the course of his entire illness he was given one 500 c.c. unit of Rh negative blood and 17,000 c.c. of Rh positive blood without reaction or alteration of his Rh negative state.

HAROLD LAUFMAN, M.D.

Curare and Intestinal Peristalsis (Curare et péristaltisme intestinal). A. DELCOURT. *Acta gastroenter. belg.*, 1950, 13: 54.

In his personal experiments the author used the barium enema to study intestinal peristalsis under the influence of curare. He took films before injection of the drug and then every 5 minutes after the twentieth minute following the injection. He used intocostrin, 1 c.c. of which represents 3 mgm. of d-tubocurarine hydrochloride and is the equivalent of 20 rabbit units. He injected this substance intramuscularly, increasing the doses without exceeding 1 unit per kilogram of body weight. With a dose of 20 units there was no change in the tonus and peristalsis of the intestine. Subjects who were given 1 unit per kilogram of body weight experienced some slight, transitory general disturbances; most of them did not feel the necessity of defecating. The study allows drawing some conclusions which are more of a theoretical than of a practical nature.

1. When given in small doses, lower than those which paralyze the voluntary muscles, curare seems to exert an action on the sympathetic nervous system. This action tends toward an increase in intestinal peristalsis. The minimal active dose lies around 20 units per kilogram of body weight, or an average of 9 mgm.; this dose is in general well tolerated. The action is not constant and has been clear-cut only in 3 of 5 cases; in addition, it is transitory and appears to be maximal about 30 minutes after the injection. It might be advantageous to use preparations with delayed action.

2. With this dosage curare does not inhibit peristalsis, and the inhibition observed by some authors can be explained by their use of higher doses, on an average from 60 to 80 mgm.

3. Curare does not change the concentration of cholinesterase in the blood. The action on the sympathetic nervous system obtained with small doses can be explained by an inhibiting effect on the autonomous sympathetic ganglions, which would create a vagal predominance. It is not impossible that larger doses may inhibit the vagal system in its turn.

4. The difference in the interpretations of the various authors depends on the variability of the action of curare, according to the dose used, and on the tonus present in the receptor at the time of the investigation.

RICHARD KEMEL, M.D.

Volvulus of the Small Intestine. CHARLES B. RIPSTEIN and G. GAVIN MILLER. *Surgery*, 1950, 27: 506.

At the Royal Victoria Hospital, Montreal, Canada, volvulus has accounted for bowel obstruction in 6.8 per cent of patients. In about one-half the cases of volvulus the small bowel was involved.

The pathology is similar in all cases. The small bowel rotates in a clockwise direction about its mesenteric axis. This results in venous obstruction, which is rapidly followed by arterial occlusion. The torsion may be intermittent at first but soon becomes fixed by edema or adhesions. Even if the mesenteric blood supply remains intact, volvulus produces a closed loop obstruction and progressive distention, and causes vascular changes in the bowel wall. The high incidence of circulatory impairment and gangrene makes a particularly dangerous form of intestinal obstruction. In this series of 23 patients

the blood supply of the involved loop was impaired in sixteen cases and resection was necessary in 8 of these.

A correct preoperative diagnosis has been established only 4 times in 23 cases. It is important for the surgeon to be aware that volvulus is a not infrequent cause of small bowel obstruction and if the condition is suspected early, operation is indicated.

Volvulus of the small intestine may occur as the result of congenital or acquired lesions. Among the congenital anomalies are abnormalities of rotation of the gut, exomphalos, Meckel's diverticulum, and congenital diverticula of the jejunum. Among the acquired lesions are peritoneal adhesions which may be postoperative, inflammatory, or tuberculous, internal hernia, foreign body impaction, tumors of the small bowel, or torsion of the intestine following gastroenterostomy.

Volvulus of the small intestine may be deceptive because repeated episodes of twisting and untwisting of the bowel give rise to intermittent symptoms.

The typical x-ray picture is that of an "arcade" loop of dilated bowel.

The treatment of choice is early laparotomy as soon as shock has been treated and fluid and electrolyte balance is restored. The type of operation depends upon the findings. In many cases detorsion and correction of the causative abnormality is all that is necessary. If gangrene has occurred, resection and primary anastomosis are preferable to exteriorization of the involved bowel. Of those patients operated upon within 12 hours, 5 recovered and 10 died. HAROLD LAUFMAN, M.D.

Volvulus of the Colon. WALTER H. GERWIG, JR. *Arch. Surg.*, 1950, 60: 721.

There exists a remarkable difference in the incidence of volvulus of the colon in the United States and that in Europe. Judging from the statistics in the literature, the incidence of volvulus of the colon is ten times as frequent in Europe as in the United States. In Europe volvulus of the colon is seen more frequently than volvulus of the small bowel, while the reverse is true in this country.

Impairment of the venous blood supply to the bowel is an early feature in volvulus, which results in damage to the wall of the bowel and marked losses in blood volume. When the viability of the bowel is thus impaired the wall becomes permeable to pathogenic organisms and toxins.

Incomplete volvulus of the cecum or sigmoid may give rise to recurrent attacks of abdominal pain and distension which are relieved by enemas, or change of position. A completely obstructing volvulus of the cecum is associated with rapidly progressing symptoms.

In the treatment of this condition, conservative measures are little more than palliative. In incomplete lesions of the sigmoid, enemas or the passage of a rubber tube under the direct vision of a sigmoidoscope may be beneficial. Surgery is necessary in the majority of cases.

F. J. LESEMANN, JR., M.D.

Concerning the Treatment of Cancer of the Low Sigmoid and High Rectum (Sur le traitement du cancer du bas sigmoïde et du haut rectum). PIERRE BERTRAND and E. C. SAUBIER. *Mem. Acad. chir.*, Par., 1950, 76: 110.

The authors think that for the cases of cancer in which conservation of the sphincter is justified the ideal intervention would be a one stage operation with the following technique:

The abdominal incision must be long: starting from the pubic spine to reach the left costal border and cutting the external edge of the sheath of the rectus, it exposes immediately the pelvic colon and allows high coloparietal detachment and liberation of the posterior aspect of the rectum in the sacral concavity down to the plane of the levators. The point where the principal artery should be ligated has been the subject of much controversy; however, the presence of adenopathy (the inflammatory or neoplastic nature of which is difficult to decide) has often led to ligature of the trunk of the inferior mesenteric artery and the authors have always noted that the upper colic stump to be anastomosed bled well. After ligation, the right leaf of the mesocolon is incised and the lower part of the incision at the level of the culdesac of Douglas joins the incision previously made on the left. Freeing of the colon is then continued to the bladder in the male and to the uterine cervix in the female.

This suffices for sigmoid cancers; for rectal and especially ampullar cancers, it is necessary to dissect the rectovaginal wall, or to separate and retract the seminal vesicles and the upper part of the prostate. When the rectum is freed down to the levator plane, the vascular condition of the colon is once more verified and the colon is cut; then the rectum is cut about 5 cm. below the tumor and end-to-end anastomosis is performed. The peritoneal continuity is restituted above the anastomosis after sulfonamide or penicillin has been deposited in contact with the repair and in the subperitoneal space. The abdominal wall is closed without drainage. Cecostomy is then performed. Finally, an incision 2 cm. long is made anterior to the coccyx, the plane of the levators is incised in the midline, and a drain is placed in the retrorectal space.

The preparation of the patient is most important since the operation must be done on an empty and disinfected intestine.

Since 1946, the authors have used this method in 23 patients with 4 deaths, or 17.8 per cent. The other 19 patients survived the operation, but late results cannot be discussed because the oldest case dates back only 3 years. Of 5 women who developed a fistula of the anastomosis, 4 healed spontaneously and 1 woman has required a permanent left colostomy; since this happened, total hysterectomy has been banned, subtotal hysterectomy being used

when necessary. The authors think that it is important not to open the vagina; no more fistulas have occurred. One man has developed a fistula which must be attributed to necrosis of the upper colic stump, probably due to thrombosis. To avoid fistula formation of the anastomosis, from 10 to 12 gm. of castor oil are now given for several days postoperatively. The cecostomy tube is spontaneously eliminated on the sixth to eighth day, and the cecostomy wound on the fifteenth day.

Although the method is applicable to most cases, Hartmann's operation is still indicated in some cases, more on the basis of general than local conditions, and in old patients. RICHARD KEMEL, M.D.

The Diagnosis and Management of Carcinoma of the Colon and Rectum. VICTOR MARCUS COPPLESON. *Med. J. Australia*, 1950, 1: 353.

In this general review on the subject of carcinoma of the colon and rectum, the author states that about 1 growth in every 4 is inoperable when first diagnosed and very few growths are discovered until they are well advanced. Usually the diagnosis is the result of an investigation prompted by symptoms, the most common of which are melena, altered bowel habit, and cramping abdominal pain. Diarrhea is one of the most common symptoms of rectal carcinoma. Failure to make a digital examination of the rectum in these cases is one of the most common causes of delay in diagnosis. A history of increasing constipation, especially if combined with abdominal pain, must be regarded with suspicion in elderly persons.

Ultimately, carcinoma of the colon or rectum is located by one of the following means: (1) by fortuitous or accidental discovery of the tumor, (2) by digital examination of the rectum, (3) by speculum and sigmoidoscopic examination, (4) by roentgenography, and (5) by the discovery of portions of growth or of carcinoma cells in the bowel.

The author suggests four rules for early diagnosis:

1. All patients aged over 40 years who present themselves with complaints of chronic painless diarrhea and the passage of blood and mucus should be regarded provisionally as suffering from carcinoma of the rectum. A careful digital examination should be made of the rectum of these patients and of all patients complaining of "piles," "chronic diarrhea," or "dysentery."

2. All patients complaining of passing dark blood, or whose feces are found to contain dark blood or clots mixed with them should be subjected to thorough digital examination of the rectum and to sigmoidoscopic and roentgenological examinations.

3. No patient should be referred for roentgenographic examination of the large bowel for a suspected carcinoma without first having undergone a digital examination of the rectum; if this examination has been omitted, it should be made by the radiologist.

4. Negative roentgenological reports for carcinoma of the colon and rectum should not be accepted as final. The examination should be repeated after a short interval if the symptoms persist.

The author makes the blunt statement that carcinoma of the bowel is a sentence of death. He tempers this statement by adding that the only effective treatment is surgery, by which death may be averted or delayed, or the patient's symptoms may be temporarily relieved.

Of all carcinomas of the large bowel, 70 per cent occur in the rectum or rectosigmoid junction. Regarding sphincter-saving operations, the author states that while saving the sphincter is highly desirable, if possible, there can be little doubt that sphincter-saving can be done only at the expense of safety. HAROLD LAUFMAN, M.D.

Anorectal Anomalies. A Statistical Study of 165 Cases with Special Reference to "Distal-Loop Trouble." CHARLES W. MAYO and ROBERTA G. RICE. *Surgery*, 1950, 27: 485.

One hundred and sixty-five patients having anorectal malformation were studied with special reference to the sex incidence of the condition, the type of the anomaly, the incidence of fistula formation, the incidence of associated congenital anomaly, the method of treatment, and the results of treatment.

There were 85 males and 80 females, of whom 70.6 per cent and 95 per cent, respectively, had rectal fistulas.

Of the males, 51.8 per cent, and of the females, 36.3 per cent had some associated congenital malformation.

The method of treatment of anorectal anomalies was dependent on the type of the anomaly and the age of the patient. If there was only a thin membrane between the proctodeum and the rectum the procedure of choice was to cut or puncture the membrane and observe the patient carefully, using repeated dilatations to avoid rectal or anal strictures. When the anus was absent but a depression or dimple was present, when one could demonstrate the presence of rectal sphincters, and also, when bulging of the blind end of the rectum could be seen, the usual treatment was a proctoplasty bringing the rectal mucosal edges to the anal skin margin. When the rectum was high, one either performed colostomy immediately or attempted a perineal exploration. Usually, in such cases a fibrous cord was found between the end of the rectum and the site of the anus. By following this, one could find the rectal mucosa, free it, and bring it down to the edges of the anal skin. However, in 12 (12.6 per cent) of the 95 cases of type 3 imperforate anus, the perineal exploration was unsuccessful. The blind end of the rectosigmoid could not be found. We believe that in the newborn male infant with a high rectum the perineal exploration should be postponed. This is especially true when there is evidence of rectovesical or rectourethral fistulas. In these patients colostomy should be performed as soon as possible and care should be used to separate the proximal from the distal barrel of the stoma. In the

newborn female infant with a rectovaginal fistula, repeated dilatations of the fistula usually sufficed until the child was old enough, and the tissues were well defined enough to allow a successful rectovaginal plastic procedure. The latter is recommended because of the relatively high incidence of urinary infections when the condition is not taken care of. When there was a congenital stricture of the rectum and anus it was usually found 2 to 4 cm. from the anus, up to the level of the mucocutaneous junction. According to David, this stricture is actually composed of mucosa and submucosa, but is often mistaken for spasm of the sphincter muscle.

Sixty-five of the patients (39.4 per cent) underwent colostomy, of whom 22 (33.8 per cent) had distal-loop trouble. A case illustrating the nature of this trouble is presented.

Good or satisfactory results were obtained in 50.3 per cent of patients and 40.6 per cent had fair or poor results. There was a hospital mortality rate of 9.1 per cent.

The authors wish especially to emphasize the importance of (1) early colostomy in the male with evidence of type 3 imperforate anus and with rectourinary fistula; (2) separation of the distal from the proximal loop of the colonic stoma in all cases in which colostomy is the preferred method of treatment.

LIVER, GALL BLADDER, PANCREAS, AND SPLEEN

Studies in Acute Cholecystitis. Cholecystostomy; Indications and Technique. FREDERICK P. ROSS and J. ENGLEBERT DUNPHY. *N. England J. M.*, 1950, 242: 359.

A plea is made for cholecystostomy in certain cases of acute cholecystitis. It is affirmed that at times the procedure may be a life-saving one which may be simply accomplished under local anesthesia. Cholecystostomy is carried out either because of unexpected technical difficulties found at operation or as a planned procedure because of the precarious condition of the patient.

Twenty cases are reported. In 12 of the patients subsequent cholecystectomy was performed, and in 6 of these the common duct was explored. Relief of the patient was remarkable with freedom from symptoms lasting as long as 4 years in 4 of the patients. There was 1 death following a second drainage of the gall bladder in a patient 74 years of age. Death was attributed to pulmonary embolism.

STEPHEN A. ZIEMAN, M.D.

Contribution to the Clinical and Anatomopathologic Study of Cancer of the Gall Bladder Without Icterus (Contribution à l'étude clinique et anatomopathologique du cancer de la vésicule sans ictère). L. DEMEULENAERE. *Acta gastroenter. belg.*, 1950, 13: 38.

Among 6,000 autopsies performed in the university service of Ghent, the author found 10 cases of cancer of the gall bladder which had not caused jaundice; these 10 cases constituted one-third of the cancers found in the biliary passages, 20 of which were tumors of the gall bladder. Two of the 10 cases are excluded from this study because their clinical data are insufficient; the other 8 are described and serve as the basis for the author's comments.

All of the cases discussed occurred in women whose ages ranged from 45 to 74 years and averaged 64 years. All of the gall bladders contained one or several calculi, but the clinical histories revealed no signs of previous cholelithiasis or cholecystitis. The exact point of origin of the cancer could not be determined in 5 cases because its evolution was too far advanced; it was thought to be in the fundus of the gall bladder in 2 cases, and simultaneously in the fundus and the neck of the organ in 1 case. The macroscopic aspect of the cancer had no relation to its microscopic form. The tumor was a glandular epithelioma, producing mucus or not, in 7 cases, and an epithelioma with epidermoid evolution in 1 case. Spread of the tumor in the liver is mostly fanshaped, but some tumors metastasize by the lymphatic route (2 cases) and some give rise to microscopic metastases in nearly all organs (2 cases).

From the point of view of the diagnosis of the nonicteric form of cancer of the gall bladder, if it is claimed that lithiasis always precedes the cancer, it must be admitted that the latter may occur without clinical manifestations of the former. The dyspeptic syndrome and loss of weight have been the only constant symptoms encountered, and even then the dyspeptic syndrome was far from being characteristic for the gall bladder and was not elective for fats. No matter how pronounced the weight loss was, it never reduced the patient to a cachectic condition. Pain was found in all forms, from simple annoyance to true colic with dorsal and scapular radiation; it was resistant to treatment. When hepatomegaly is found, it is already a sign of the implacable evolution of the disease; it is limited to the right lobe which is hard and irregular, and has a sharp border. A subhepatic tumor is sometimes palpable without increase in the volume of the liver; if it is due to the gall bladder, its mobility must be investigated by change of position of the patient from right lateral to left lateral decubitus. The most important laboratory finding is the absence of B bile in the fluid obtained by duodenal drainage. Moderate leucocytosis found even in the absence of any sign of infection is a useful finding. Roentgen examination may contribute to the diagnosis; the gall bladder does not become opaque after the ingestion of contrast substance. The microscopic metastases of some forms of cancer may be found in smears of the sternal marrow. No relation was found between the anatomic type of the tumor and the clinical form of the disease.

Complications may be local and consist of a purulent cholecystitis or a biliary peritonitis from perforation, or they may be due to metastases causing destruction of the hepatic substance, grave anemia,

ascites, pulmonary infiltrations and their results, and even diabetes by massive invasion of the pancreas.

Treatment is surgical, but it will never be possible to state with certainty that the operation, no matter how radical it may be, has cured the disorder.

RICHARD KEMEL, M.D.

A Large Cystic Collection in the Lesser Peritoneal Sac Following Subacute Necrotic Pancreatitis (Volumineuse collection enkystée de l'arrière cavité des épiploons consécutive a une pancréatite nécrosante subaigue). MARCEL ROUX, CH. DEBRAY, and ET. BERNIER. *Sem. hôp. Paris*, 1950, 26: 805.

This cyst was first treated by marsupialization. The fluid obtained did not contain lipase or amylase, but traces of trypsin. Histologic study of a fragment of the wall revealed fibrous tissue without epithelial covering; thus it was a false cyst. The secretion soon stopped and the drain was removed at the end of 1 month; the opening closed rapidly. Three months later there was a recurrence.

At the second operation, more than 2 liters of brownish sanguineous fluid were found in the pocket, exploration of which revealed in the area corresponding to the pancreas a necrotic zone in the form of a transverse band, slightly ascending to the left, which was 10 cm. long and 4 cm. wide. There was a sort of fetid, brown greenish magma that was of slightly pasty consistency and could be removed in pieces. There were no free necrotic masses in the cavity. The wall was carefully closed around a large drain which was kept in for 3 months, after which time the cavity seemed to be reduced to practically nothing. However, the fistula persisted and, for fear of another recurrence, it was decided to anastomose the fistula to the stomach. Recovery from this operation was uneventful. The patient has regained his weight and resumed his occupation. From time to time he has a painful attack in the left hypochondrium; these attacks are not violent but are accompanied by swelling and hardening of the subcostal region with a temperature rise to 39° or 40°C. This condition persists for 2 or 3 days and then disappears spontaneously.

Although some authors have not hesitated to drain collections of several liters into the stomach into the duodenum, recourse to such a method seemed illogical in the present case, nor did it seem advisable to use the procedure recommended by Achmatowicz—draining the cavity into a jejunal loop with Y anastomosis. It appeared to be more logical to perform a second marsupialization with the deliberate view of performing a fistula anastomosis if the pocket did not disappear. The fistula anastomosis is itself only a makeshift, and cases have been reported in which obliteration of the fistula has finally led to recurrence of the cyst. Although in the present case it has not been possible to demonstrate roentgenologically the permeability of the fistulogastric anastomosis, it must continue to function intermittently since the patient has occasional crises which disappear spontaneously. The authors think that when the lesion originates in the region of the tail or left portion of the pancreas, the most satisfactory therapeutic method would be resection of the diseased pancreas, which alone could lead to cure by stopping the fluid secretion.

RICHARD KEMEL, M.D.

Surgical Procedures for Pancreatic Lesions. Review of Pancreatic Surgery. RALPH F. BOWERS. *Arch. Surg.*, 1950, 60: 817.

This article is a comprehensive review of the various diseases of the pancreas for which surgical therapy is of value. In the vast majority of the cases of acute pancreatitis there is associated infection of the biliary tract, biliary lithiasis, or abnormal communication between the common and pancreatic ducts. The blood amylase test is the most important laboratory test in establishing the diagnosis. There is no question that the avoidance of early operation has materially reduced the mortality of this condition. The author strongly advocates the use of paravertebral sympathetic blocks in the conservative treatment; it is usually necessary to block the ninth through the twelfth thoracic segments. In the advent that laparotomy is performed the author advocates drainage of any pancreatic abscesses that may be present and removal by cholecystotomy or choledochotomy of any stones that are present.

The more obscure condition of chronic pancreatitis presents a difficult therapeutic problem. Cholecystectomy and choledochotomy should be performed on proper indication if biliary tract disease is present; this will be curative in some patients. Operative cholangiograms should be taken and if these demonstrate regurgitation of the dye into the pancreatic ducts one of three methods is available for relief: (1) resection or transection of the sympathetic fibers supplying the region; (2) instrumental dilatation of the sphincter of Oddi or severance of its muscular fibers; and (3) shunting operations such as choledochojejunostomy, duodenostomy, or gastrostomy. However, cholangitis is a complication of such a procedure and may be more dangerous than the original condition. The author advocates the utilization of a choledochojejunostomy by means of the Roux-Y principle.

Benign pancreatic cysts may arise in any part of the pancreas. The proper surgical treatment of these lesions is marsupialization, resection, or internal drainage. Cystadenomas of the pancreas, because of the danger of malignancy, should be excised unless the operative risk is too great. Because of their consistency, it is often most difficult to locate islet cell adenomas at operation; if the tumor cannot be found, resection of the distal two-thirds of the pancreas should be performed.

Fifty-six per cent of the patients with carcinoma of the head of the pancreas have pain. Infectious hepatitis must be carefully excluded in the differential diagnosis; the gall bladder is rarely enlarged in this condition and the cephalin flocculation, thymol turbidity, and sulfobromphthalein tests are usually

positive. The author advocates the radical operation in only the most favorable cases. It is very difficult to diagnose carcinoma of the body and tail of the pancreas at an early stage. The symptomatology of carcinoma of the tail of the pancreas may consist of chills, fever, and loss of appetite and strength, as well as an enlarged spleen, a picture that may closely simulate that of an infection or Hodgkin's disease. F. J. LESEMANN, JR., M.D.

Splenectomy in a Case of Lymphogranulomatosis Benigna (Schaumann) (Splenektomie bei einem Fall von Lymphogranulomatosis benigna [Schaumann]). ERIK MILLBOURN. *Acta med. scand.*, 1950, 137: 20.

The case of Schaumann's lymphogranulomatosis benigna here reported was that of a 53 year old woman who had been suffering for about a year from exhaustion, anorexia, vomiting, and loss of weight. The spleen was enormously enlarged and there was a moderate grade of anemia and mild fever, and cutaneous ecchymosis. On one occasion a course of penicillin produced considerable improvement in the general condition and a considerable decrease in the size of the enlarged spleen.

Splenectomy was done and at this operation, in addition to the huge spleen, there were observed soft, pigeon-sized lymph node enlargements along the splenic blood vessels and at the porta hepatis. In the course of excising the spleen the tail of the pancreas was found to be firmly adhered to the splenic hilus. In separating these adhesions some damage was done to the tail of the pancreas itself. In the postoperative period there was some tendency toward subfebrile temperature and the drains alternately discharged pancreatic secretions. Following the removal of the drains a pleuritis developed on the left side, probably as a result of the stagnation of pancreatic secretions in the region of the operation. Thoracocentesis was done.

It is now almost 2 years since the splenectomy was done. During this period the patient was under treatment with arsenic, iron, and ultraviolet radiation. She has constantly gained in weight and strength and the anemic condition has improved.

Histologic examination of the removed spleen, which weighed 2.1 kgm., showed macroscopically that the spleen consisted of lymphatic tissue permeated by granular structures resembling rice bodies. The microscopic study of the splenic tissue disclosed an exuberant white pulp with numerous large lymph follicles frequently exhibiting huge reaction centers. In these centers numerous eosinophils were present, also hyaline bands and agglomerations of hyaline granules. The stain for amyloid was negative. In the extremely cell-rich red pulp were numerous plasma cells in various stages of development, and here also were numerous eosinophils. In addition, there were observable numerous collections of confluent or isolated, roundish foci of tuberculoid structure, composed of epitheloid cells, and numerous giant cells of the Langerhans type. There was no evidence anywhere of necrosis. In places these foci contained collagen fibrils and in many places they were surrounded by collagenous connective tissue. On the periphery of these foci were evident in places collections of round cells among which could be seen not a few plasma cells. The 2 biopsy specimens of the enlarged lymph glands previously described contained largely identical findings with the spleen.

The histological diagnosis was granulomatous inflammation of the type seen in Schaumann's disease.

Of course, the time has been too short (2 years) to speak of definitive cure by splenectomy in Schaumann's disease. There are still two unpleasant possibilities to be considered. The first possibility is that the spleen was exercising an abnormal depressive influence on the blood-forming organs and its removal permitted of temporary recuperation of the blood, without cure of the original disease process. The other possibility is, of course, the outbreak of a tuberculous process somewhere else in the body.

JOHN W. BRENNAN. M.D.

MISCELLANEOUS

Right Diaphragmatic Hernias of Pseudotumoral Form. Contribution to Study of Opacities of Abdominal Origin at the Right Base (Les hernies diaphragmatiques droites à forme pseudo-tumorale. Contribution à l'étude des opacités de la base droite d'origine abdominale). E. CURTILLET and R. AUBANIAC. *J. chir.*, Par., 1950, 66: 257.

Four conditions may produce opacities simulating tumors at the right base of the chest: (1) hernia of the liver, (2) certain atypical shapes of the liver, (3) tumors of the liver, especially hydatidiform cysts, and (4) hernias through Larrey's fissure, containing omentum. The last mentioned condition is hardly known.

The authors observed 2 such cases, both in men, 36 and 47 years of age, respectively. The first patient was complaining of air hunger and cardiac palpitations. Roentgenograms revealed a homogeneous shadow occupying two-thirds of the median portion of the lower half of the right chest. Pictures taken after the institution of a pneumothorax demonstrated a clear space between the shadow and the diaphragm. The chest was entered through the bed of the right sixth rib. The herniated portion of the omentum and the sac were resected and the hernial ring closed.

The second patient entered the hospital with edemas of the lower extremities. A shadow, similar to that in the first case, was discovered in the right chest at roentgenographic examination. Pneumoperitoneum was instituted and subsequent pictures confirmed the diagnosis of a diaphragmatic omental hernia which was repaired by means of the abdominal approach.

Such hernias are due to a dehiscence of the diaphragm, of congenital or acquired origin. They cause vague complaints or may be asymptomatic.

The shadow is located in the right cardiodiaphragmatic angle, just behind the costal arch. Pneumoperitoneum has a greater diagnostic value than pneumothorax.

The authors report cases, illustrating the other aforementioned 3 conditions which may produce opacities at the base of the right half of the chest.

The abdominal approach should be used for the repair of epiplocele (omental hernia) through Larrey's fissure. JOSEPH K. NARAT, M.D.

Gastric Protrusion through the Esophageal Hiatus (Les protrusions gastriques à travers l'hiatus oesophagien). M. BROMBART, J. GOUTKINE, and Y. LAURENT. *Acta gastroenter. belg.*, 1950, 13: 22.

In contradistinction to earlier beliefs, modern methods of roentgenologic examination have shown that herniation of the stomach through the esophageal gap is quite frequent, especially in obese patients over 50 years of age.

The authors discuss the anatomy of the esophageal hiatus, the different types of hernias, and the etiology, pathogenesis, and symptomatology of the condition, and describe a number of cases of their own observation.

They differentiate three types:

1. Bradyesophagus, in which a portion of the stomach is permanently situated above the diaphragm. This rare condition is not a hiatus hernia in the strict sense, but a congenital ectopy. The esophagus is too short, the thoracic part of the stomach is covered by peritoneum, and there is no sac.

2. Paraesophageal hernia. The esophagus is of normal length, its inferior end is below the diaphragm, and the stomach is herniated laterally to the esophagus, either to the right or to the left, in the posterior mediastinum.

3. Gastric hernia, in which the esophagus is of normal length but its inferior end lies above the hiatus.

In the last two types there is a sac.

In addition to these three types there occur transitory, intermittent protrusions of small portions of the stomach through the hiatus. This condition is called hiatus insufficiency and is frequent in old persons. There is no consensus of opinion whether or not these intermittent forms cause any clinical symptoms.

As mentioned, the age factor plays an important role in the pathogenesis. Loss of elasticity in the tissues of the hiatus membrane and decrease of muscular tonus of the diaphragm may bring about the condition, especially in obese patients. Furthermore, the affection occurs in the later part of pregnancy, in ascites, and in cases of large abdominal tumors. It can be precipitated by an attack of coughing or by emesis.

The outstanding symptom is retrosternal pain, often simulating an attack of angina pectoris. The pain may irradiate into the left shoulder and arm. Also dysphagia and dyspnea occur in some cases. The complaints are aggravated in the supine position, and relieved by standing.

It is remarkable that hiatus hernia is often associated with other affections of the gastrointestinal system such as cholecystitis, cholelithiasis, diverticulosis, peptic ulcer, and others. Twenty-six of the 39 cases of the author's observation showed 1 or more of these conditions associated with hiatus hernia.

The diagnosis is clinched by roentgenologic examination. However, the hernias are hard to visualize because a great deal of experience and special roentgenologic technique are required. The author discusses the technique in great detail. Pictures should be taken in different positions, especially in the Trendelenburg position.

In the differential diagnosis the problem often arises whether anginous attacks are due to the hernia or to a concomitant cardiovascular affection.

WERNER M. SOLMITZ, M.D.

GYNECOLOGY

UTERUS

Adenocarcinoma of the Uterine Corpus. Diagnostic and Therapeutic Considerations (L'adénocarcinome du corps utérin. Considérations sur le diagnostic et le traitement). LÉOPOLD MAYER and CHARLES MAYER. *Acta chir. belg.*, 1950, 49: 199.

The great improvement of results in the treatment of adenocarcinoma of the uterine corpus in the last 15 years is attributable to an earlier diagnosis, better methods of anesthesia, and roentgen and radium therapy.

During a 9 year period the authors observed 76 cases of cancer of the body of the uterus and 212 cases of cancer of the cervix. The patients' ages ranged from 39 to 75 years.

From the pathologicoanatomic viewpoint, diffuse and circumscribed forms of adenocarcinoma may be distinguished.

Cancer of the body of the uterus has a tendency to invade the lymphatics accompanying ovarian blood vessels.

If the examination of the cervix fails to disclose the cause of postmenopausal hemorrhage, adenocarcinoma of the body of the uterus is responsible for metrorrhagia in 50 per cent of the cases. Diagnostic curettage and Papanicolaou's method of examination of vaginal smears help to identify the condition.

Abdominal total hysterectomy is advocated by the authors. Five year cures were obtained by them in 76 per cent of a series of 50 patients. The operation is supplemented by x-ray and radium therapy.

JOSEPH K. NARAT, M.D.

A Statistical Report of 955 Cases of Cancer of the Cervix Uteri and 321 Cases of Cancer of the Corpus Uteri. W. L. HARNETT. *Brit. J. Cancer*, 1949, 3: 433.

In 1938 and 1939, the Clinical Cancer Research Committee of the British Empire Cancer Campaign carried out a clinical survey of all cases of cancer seen in the hospitals in the administrative county of London. During this period, 15,203 cases of cancer were registered. There were 955 cases of cancer of the cervix and 321 cases of cancer of the corpus uteri. The patients have been followed for 5 years or more.

Of the 955 patients with cancer of the cervix, 95 per cent were married or widowed. Of the married group, 90 per cent had children. The first symptom of cervical cancer was irregular hemorrhage in 67.5 per cent of patients and vaginal discharge in 20 per cent. Forty-five per cent of these women consulted a doctor within 3 months of noting the first symptom; 20 per cent consulted a doctor within the next 3 months; in 25 per cent, the delay before seeking advice was longer than 6 months, and 27 patients delayed seeking advice for over 2 years. A vaginal examination was done at the first visit in 70 per cent of the patients, and in only 10 per cent was the examination delayed longer than 1 month. Proper treatment was advised in all except 3 per cent of the cases.

The cervical cancer was described as: stage 1 (League of Nations), 23.4 per cent; stage 2, 37 per cent; stage 3, 25 per cent; and stage 4, 15 per cent. The 5 year survival rate for all cases was 27.7 per cent. Of the 238 survivors, 10 have died of cancer within 10 years.

In stage 1 cancer of the cervix, hysterectomy gave the best results, which were slightly improved if the operation was preceded by treatment with radium. The results obtained with radium were almost as good as those of surgery, but were not improved by courses of x-ray treatment in addition.

In patients with stage 2 lesions, both the 5 year survival rate and the expectation of life were better after radium therapy than after surgery, and with preliminary x-ray therapy the results were slightly improved.

Almost all of the patients with stage 3 lesions received radium, and the addition of x-ray treatment either before or after radium improved the results.

Carcinoma of the corpus was seen more frequently than cancer of the cervix in single and multiparous women. Five per cent of these patients gave a history of suffering from uterine fibroids; in 10 per cent of the patients fibroids and cancer of the corpus occurred simultaneously. Irregular hemorrhage was the first symptom in 63 per cent. Only 33 per cent of patients consulted a doctor within 3 months of noting the first symptom; 36 per cent waited more than 6 months and 17 women delayed more than 2 years. In only 4 per cent of patients was a vaginal examination delayed longer than one month. All but 2 per cent were referred for treatment following the initial examination. The cancer was limited to the uterus alone in 65 per cent of patients at the time of hospital admission.

The 5 year survival rate for all cases of cancer of the corpus was 44 per cent. Two of the 127 survivors of cancer died within 10 years. Where the cancer was limited to the corpus, the best results were obtained by hysterectomy with excision of the tubes and ovaries. These results were not improved by the addition of radiotherapy. Supravaginal hysterectomy gave a poor survival rate, which was improved slightly by the addition of radiotherapy.

JOHN R. WOLFF, M.D.

Complete Abdominal Hysterectomy. A Simplified Technique and End Results in 500 Cases. ALBERT H. ALDRIDGE and RICHARD S. MEREDITH. *Am. J. Obst.*, 1950, 59: 748.

We now have techniques for complete removal of the uterus by the abdominal route, which in the

hands of competent surgeons are as safe as those for the subtotal operation. Results from the utilization of the authors' technique by a group of gynecologists and hospital residents show that it is a simple, safe method for complete hysterectomy. In a series of 500 cases, the 2 operative deaths reported were due to emboli. Morbidity was exceedingly low.

Complete removal of the uterus as a nearly routine procedure may prevent later development of an occasional carcinoma in a cervical stump. At least 4 of 5 cervices removed from women who have indications for hysterectomy will show unhealed birth injuries, chronic inflammation, or an occasional unsuspected malignant growth.

The incidence of postoperative pelvic complaints and the frequency and severity of menopausal symptoms are less after complete removal of the uterus than after subtotal hysterectomy.

The technique of total hysterectomy is not an original one but is simply a combination and modification of various steps which have been described previously by many gynecologists. It has been finally adopted by the Staff of the Woman's Hospital, New York. JOHN R. WOLFF, M.D.

ADNEXAL AND PERIUTERINE CONDITIONS

The Histogenesis of Brenner's Tumor (Histogénèse de la tumeur de Brenner). SIMON LAUZÉ. *Union méd. Canada*, 1950, 79: 250.

Three theories regarding the histogenesis of Brenner's ovarian tumors vie with one another: according to one theory, the tumor originates from Walthard's vestigial tissue; another theory maintains that the tumor derives from the mesonephron; and the third theory claims that the tumor develops from the lining epithelium of the ovaries.

There is a striking resemblance between the epithelium (1) of Brenner's tumor, (2) of Walthard's islets in the ovarian hilum and in the wall of the tubes, and (3) of von Brunn's glands located at the level of the prostatic urethra.

The bifid nucleus, characteristic for Brenner's tumor, is not a sign of cellular division. Similar formations are found in the germinative epithelium of the ovaries, in the uterine collum, in a certain type of glandular epithelioma of the corpus uteri, and in the epithelium of urinary excretory ducts. If Brenner's tumor were a derivative of the germinal epithelium, it would at least occasionally contain cystic, glandular, or papillary formations, but this is never the case.

The author concludes that Brenner's tumor derives from the mesonephron. JOSEPH K. NARAT, M.D.

Theca Cell Tumors. With a Report of 12 New Cases and Observations on the Possible Etiologic Role of Ovarian Stromal Hyperplasia. WILLIAM H. STERNBERG and CORNELIA J. GASKILL. *Am. J. Obst.*, 1950, 59: 575.

Clinical and pathologic data on 12 additional cases of theca cell tumor of the ovary are presented. Adenocarcinoma of the endometrium was present in 1 case, atypical hyperplasia of the endometrium (premalignant in character) in another, and carcinoma *in situ* of the cervix in a third. This strongly suggests that estrogen plays an important, although not a lone, role in the pathogenesis of endometrial carcinoma. Unusual clinical findings included a case of pregnancy with death at parturition due to rupture and hemorrhage from the tumor pedicle, a case in which the symptomatology simulated pregnancy, a case of endometriosis in a woman 11 years after the menopause, and an instance of associated aleucemic lymphatic leucemia.

Examination of the non-neoplastic ovarian tissue in the same or opposite ovary revealed a significant degree of ovarian stromal hyperplasia in all 8 patients in the fourth decade and beyond, in whom tissue was available for study. The high incidence of ovarian stromal hyperplasia and other evidences of stromal activity in the non-neoplastic ovarian tissue suggests that the theca cell tumor may develop against a background of diffuse ovarian stromal stimulation.

The age incidence of theca cell tumors parallels that of ovarian stromal hyperplasia and ovarian fibromas. The urinary gonadotropin was elevated in 1 postmenopausal patient with clinical evidence of estrogenic activity of the theca cell tumor.

GEORGE BLINICK, M.D.

Ovarian Carcinoma Arising in Endometriosis. GEORGE W. CORNER, JR., CHIH-YUAN HU, and ARTHUR T. HERTIG. *Am. J. Obst.*, 1950, 59: 760.

Proved cases of ovarian carcinoma arising in endometriosis are exceedingly rare. In a study of 889 cases of ovarian endometriosis and 265 ovarian malignancies occurring in a 45 year period at The Free Hospital for Women, 3 undoubted cases of this type were found which are to be added to the 8 cases previously reported in the literature. In addition, 3 highly probable cases are also reported.

The probable precursors of carcinoma arising in endometriosis are also rare. True papillary projections have occurred in only 5 endometrial cysts and anaplasia only 6 times. There was 1 case of pseudomucinous cystoma (benign) arising in an endometrial cyst.

In the course of this study 9 cases were encountered which strongly support the celomic metaplasia theory of the origin of endometriosis. These cases, in which endometriosis arose from germinal epithelial elements, also strongly suggest that serous and even pseudomucinous cysts arise from ovarian germinal epithelium.

Carcinoma may arise in association with endometriosis by two means. The first, exemplified by cases in which mixed types of epithelium are found, is by malignant changes in the nonendometrial portions of these mixed cysts. Examples seen include the benign pseudomucinous cystoma, a pseudomucinous cystadenocarcinoma probably arising in an endometrial cyst, and a serous cystadenocarcinoma defi-

nitely arising in close proximity to endometriosis. The second is by malignant transformation of endometriosis, as in 1 probable and 1 definite case of papillary adenocarcinoma and 1 definite case of adenoacanthoma of this origin. JOHN R. WOLFF, M.D.

MISCELLANEOUS

The Morphology and Pelvic Inclination in the Genesis of Genital Prolapse (Morfologia e inclinazione della pelvi nella genesi del prolasso genitale). MARIO CARBONINI. *Ann. ostet. gin.*, 1949, 71: 659.

A hundred and eight patients suffering from genital prolapse were observed at the Obstetric and Gynecologic Clinic of "Luigi Mangiagalli" at Milan, Italy, during the 2 years, 1948 and 1949. Without belittling the role of constitutional inferiority of the muscular and fascial tissues, or "asthenia universalis" in genital prolapse, the author believes, on the basis of the numerous reports on this subject by the German and Italian schools of thought, that the morphologic and static aspects of the female pelvis should be assigned a pre-eminent position in any theory of genital prolapse.

With the purpose of presenting more exact statistical evidence in support of the afore-defined theories the author made an exhaustive study of the 108 cases mentioned. In addition to obtaining the evidence of tissue asthenia by clinical observation of his material, the author made exhaustive measurements of the pelves of these patients. The diameters measured were the distances between the anterior superior iliac spines and crests, the bitrochanteric diameter, the conjugata externa, the right and left oblique diameters, and the coccisubpubic and bi-ischiatic diameters; the circumference of the pelvis was also measured. Finally, the pelvic inclination was measured by means of the ileocoxometer, or ileococcic leveller, constructed by the author himself. The values procured by these measurements are presented as typical, or modal, values.

By means of the manipulation of these values it is shown that in the vast majority of the patients the transverse measurements were noticeably, at times markedly, greater than those to be expected in the normal pelvis, while the anteroposterior measurements were less. This would, of course, at once suggest the presence of a flat pelvis; however, the condition is not a simple acquired flat pelvis, but has many peculiarities suggesting a constitutional basis for the deformity.

Most striking were the measurements on the pelvic inclination. While the normal angle which the pelvis makes with the long axis of the body lies between 55 and 60 degrees, in this material there were 72 patients in which the angle of the pelvic inclination was less than normal, and only 10 patients in which it was greater. There were 23 instances in which the angle ranged between 40 and 50 degrees. This pelvic posture in which the superior strait tended to assume a more nearly level posture could, in these longilineal microsplanchnic individuals, be easily appreciated with the naked eye. The pelvis was wide, the thighs were closely approximated, the external genitalia were abnormally visible, and there was practically no evidence of lumbar lordosis.

The author regards the so-called "hypertrophied" cervix in these patients as a congenital, or hereditary, failure of the infantile type of uterus to assume the adult form. The wide and flattened pelvis favors the retroposition of the uterus—which is designated the first stage in the genital prolapse. The roomy pelvic framework leads to a separation and weakening of the supporting tissues of the pelvic diaphragm. The prolapse, therefore, is largely due to faulty static and morphologic conditions in an individual with inferior tissue resistance on a hereditary basis. To this genotypic factor are added the phenotypic factors of faulty posture and faulty habits of muscular functioning. JOHN W. BRENNAN, M.D.

Researches on the Hormonal Control of the Formation of Sex Organs in the Rabbit, and Remarks on Certain Malformations of the Genital Tract in Man (Recherches sur le controle hormonal de l'organogenèse sexuelle du lapin et remarques sur certaines malformations de l'appareil génital humain). ALFRED JOST. *Gyn. obst.*, Par., 1950, 49: 44.

The development of the sex organs takes place in three stages: (1) differentiation of the gonads, (2) differentiation of the primary sexual organs, and (3) development of the secondary sexual traits. The first two of these stages occur during embryonal life, the third stage occurs at puberty.

During the last 15 years much experimental work has been done to determine if, and to what degree, the development of the genital tract is influenced by hormones secreted from the gonads. Sex hormones were introduced either directly into the embryos of monkeys and guinea pigs, or injected into the pregnant mother to reach the embryo via the placenta.

Whereas it is possible to change the sex of the gonad by the injection of sex hormones in frogs and birds, this has never been demonstrated in mammals. In the latter, treatment of the mother with high doses of sex hormones before the time of differentiation of the genital tract produces various forms of sex intergrades in the embryo without reversing the sex of the gonad. These changes of the internal and external genital organs produced during the embryonal period are irreversible.

The fact that it is possible to modify the formation of the genital organs by hormonal treatment of the embryo does not prove that normal organogenesis is subject to the control of hormones produced by the embryonal gonads. To study this question, as well as the role of the pituitary gland, the author performed extremely interesting experiments on rabbits. He castrated the embryos at different stages of development and observed the influence that the castrations had on the formation of the genital tract.

Gravidity in rabbits takes from 30 to 31 days. The gonads appear at the 15 days' stage, and differentiation of the genital tract sets in at 20 days.

Whereas in female embryos castration between the twenty-first and twenty-third days made little or no difference in the formation of the genital organs, castration of male embryos before the differentiation caused the development of female internal and external sex organs. No male sex character appeared in these cases if castration was performed between the nineteenth and twenty-first days of gravidity. In these cases the wolffian bodies regressed, and the Mueller organs persisted and continued to develop into oviducts, the uterus, and the vagina. At the end of the fetal period, these embryos were practically identical with females. When castration was performed on the twenty-second or twenty-third day, a mixture of male and female organs of various degrees resulted. Castration of male embryos after the twenty-third day did not cause any change in the male development.

After unilateral castration the results varied. In some cases the remaining testicle was sufficient to produce persistence and development of both wolffian organs; in others different degrees of pseudohermaphrodism resulted.

A testicle graft in a female embryo produced an intersexual genital tract, comparable to that of certain natural hermaphrodites.

The role of the hypophysis was tested by decapitation of the embryo before the onset of sexual differentiation. The operation causes testicular insufficiency and pseudohermaphrodism in the rabbit; this, however, can be prevented if, at operation, gonadotropic hormone is administered to the embryo.

The fact that absence or insufficient activity of the testicles produces female development of an originally male embryo permits certain conclusions on pseudohermaphrodism and other anomalies of the genital tract in man. Male pseudohermaphrodism can be interpreted as functional deficiency of the testicle during the embryonal period. Female pseudohermaphrodism may be linked to adrenocortical hyperplasia during the embryonal period.

Numerous other interesting observations and theories are discussed in this article. They should be read in the original. WERNER M. SOLMITZ, M.D.

Methods and Results in 117 Cases of Amenorrhea Treated with Gonadotropic Hormones. OVE RIISFELDT. *Acta obst. gyn. scand.*, 1950, 29: 255.

The methods of treatment and results in 117 cases of amenorrhea treated with gonadotropic hormone are reported.

By means of successive treatment with serum (equine) gonadotropin and chorionic gonadotropin it is possible in the great majority of cases of secondary amenorrhea to restore the function of a resting ovary, at least temporarily. It is found that the most effective form of treatment is as follows: "antex" (serum gonadotropin) 3,000 I.U. daily for 5 consecutive days, followed by "physex" (chorionic gonadotropin) 1,500 I.U. every other day, 3 injections in all. The menstrual flow will generally appear from 8 to 10 days after the last "physex" injection.

Treatment with gonadotropic hormone in the form employed stimulates the maturing of the ovarian follicles and produces ovulation and corpus luteum formation, and the endometrium reflects the functional state of the ovary. Occasionally, an overstimulation of the ovary is seen, which will induce diffuse luteinization and enlargement of the ovaries. Most frequently the condition subsides quickly; at any rate, really serious complications of this kind are very rare.

With treatment of the type stated here (the dosage used in the present material has varied somewhat), it is found that in the various groups the chances of lasting results of the treatment, i.e., continued regular menstrual cycles, are roughly as follows:

Secondary amenorrhea of up to 2 years' standing: approximately, the condition will continue with regular menstrual cycles after the treatment in one-half of the cases.

Secondary amenorrhea of several years' standing: the condition will continue with regular menstrual cycles in less than one-half of the cases. When a patient fails to react to the first treatment, a further attempt should be made.

Primary amenorrhea: the chances are, on the whole, very poor. It is of decisive importance whether the patient's body type is influenced by the endocrine dysfunction or not. In the former case, there seems to be very little chance of successful results. For patients with a normal feminine body type the chances are not decidedly poor; it may be possible to induce regular menstrual cycles in a small number of these patients.

Hormonoanalytic examinations have shown that in patients who excrete increased amounts of gonadotropic hormone (the hormonal castrate type) the chances are decidedly poor.

It is mentioned that pregnancy may often follow the treatment for amenorrhea in formerly sterile patients.

Fifty-five per cent of the amenorrheic patients had a normal metabolism, while the others, with a single exception, had hypometabolism.

It was not possible to demonstrate any difference in the effectiveness of the gonadotropin treatment whether the patient had normal metabolism or not. On the other hand, it appears that thyroidin treatment alone was without effect on the amenorrhea in the author's patients. CHARLES BARON, M.D.

Abnormal Bleeding in Obstetrical and Gynecological Conditions. CLARENCE A. LATHROP, WILLIAM J. DIECKMANN, and J. GARROTT ALLEN. *Am. J. Obst.*, 1950, 59: 897.

Recent reports by Allen and his coworkers show that in many conditions complicated by hemorrhage, there is an abnormality which may be detected by the titration of heparinized blood with protamine. This is a report of an investigation on patients who exhibited bleeding or bleeding tendencies associated with various obstetrical and gynecological conditions, including normal pregnancy and delivery. The method of study included the determination of: (1)

the protamine titration, (2) the whole blood clotting time, (3) the thrombocyte count, (4) the prothrombin activity, and (5) the gross observation of clot retraction and fibrinolysis. In some of the cases in which active spontaneous bleeding was present and an increased protamine titration was demonstrated, treatment with the antiheparins, toluidine blue, protamine sulfate, or both, was instituted.

There is often an increased protamine titration in normal pregnancy before delivery which returns to normal early in the puerperium. The presence of an increased titration does not predict abnormal bleeding in pregnant women at delivery or in the puerperium.

It should be pointed out that there are many causes of postpartum hemorrhage. These include: (1) retained placental tissue, (2) uterine atony, (3) lacerations, (4) tumors, (5) conditions of the blood such as thrombocytopenia, an excessive amount of fibrinolysin, hypoprothrombinemia, and fibrinogenopenia.

If an increased protamine titration is present in a bleeding patient in whom no other demonstrable pathological cause is present, clinical trial of protamine sulfate, toluidine blue, or of both is indicated.

Cases have been presented which indicate that if the afore-mentioned abnormality is present as evidenced by an increased protamine titration, and other causes for bleeding have been ruled out, a clinical trial of protamine sulfate, toluidine blue, or of both is indicated. No ill effects from the use of protamine sulfate have been noted except muscular soreness at the site of injection; however, it must be injected deeply into the muscles. Transient nausea may occur in about 20 per cent of the patients receiving toluidine blue. When this dye is given intravenously, precautions must be taken that there is no extravasation and that the injection is given slowly. Toluidine blue has a more prolonged action than protamine sulfate. CHARLES BARON, M.D.

Endometriosis. BENTLEY P. COLCOCK and TIMOTHY A. LAMPHIER. *Ann. Surg.*, 1950, 131: 507.

Endometriosis is one of the most common conditions affecting the female pelvis, yet it frequently escapes detection as a cause of pelvic pain. Many patients have lower abdominal discomfort and pain for years before endometriosis has developed to a point where the diagnosis is obvious. In the lower income group where marriage tends to take place at an earlier age and the number of children per marriage is greater, endometriosis is much less frequently encountered.

In spite of the interest of many competent observers over a period of years, the etiology remains obscure. Regardless of the origin of the ectopic endometrium it is identical histologically and physiologically with normal endometrium. The cyclic bleeding that occurs produces irritation and inflammation in the surrounding tissues, with resulting cyst formation. Endometriosis most commonly involves the ovaries and pelvic peritoneum, but may involve any abdominal organs, and has even been found in abdominal and mediastinal lymph nodes. The extensive adhesions which occur may result in partial or complete intestinal obstruction.

The classical picture of endometriosis is a woman between the ages of 30 and 40 who is either childless or who has had but one pregnancy and complains of increasing dysmenorrhea. In this series of 370 patients, 48.6 per cent were sterile as compared to the general sterility rate of 22 per cent in this age group. The most common physical finding was the presence of tender nodules in the cul-de-sac, along the uterosacral ligaments, and on the posterior surface of the uterus. In this series 213 patients were operated upon, with a correct preoperative diagnosis of endometriosis in 55 per cent.

When symptoms are mild they are controlled by medical management. Surgical treatment should be individualized. The chief problem is whether or not castration is necessary. There is an increasing tendency in recent years toward the use of conservative operative procedures, the procedure depending on the symptoms and pelvic findings. Large chocolate cysts should be removed, fixed retroverted uteri mobilized and suspended, and, in so far as possible, all endometrial cysts excised. Sixty-three and nine-tenths per cent of the patients in this series, however, were subjected to radical surgery. The authors do not believe that roentgen ray therapy is indicated.

ELY ELLIOTT LAZARUS, M.D.

OBSTETRICS

PREGNANCY AND ITS COMPLICATIONS

Studies on Erythroid Elements and Serum Iron in Normal Pregnancy. LUNDSTRÖM. *Upsala läk. fören. förh.*, 1950, 54: 1.

This monograph is one of the most exhaustive ever written on this subject. The author and his coworkers have endeavored to clarify many controversial points. The essay is divided into eight separate chapters covering some 80 pages. The first chapter is devoted to a review of the literature with regard to certain blood findings which he thinks are most important.

Among other subjects reviewed are (1) erythroid elements and hematocrit in pregnancy and postpartum, (2) serum iron in pregnancy and postpartum, (3) plasma volume and iron in pregnancy, (4) iron metabolism in pregnancy, and (5) anemia in pregnancy.

The author's laboratory experiments were directed toward two main points: (1) the changes in certain blood findings such as hemoglobin and red blood count, hematocrit, corpuscular value, and serum iron content, and (2) the effects of parenteral iron administration upon these values.

The second and third chapters are devoted to the material, techniques, and statistical method. A comparison was made of the author's own normal material with that of other investigators. He found consistently that in his material the red blood count, hemoglobin, and serum iron were different from those obtained by other observers in the same country. He concluded, however, that because of different techniques and technical errors, these discrepancies were of no great consequence. The author points out that many investigators have determined a lower limit of hemoglobin below which the diagnosis of anemia is established. In pregnancy, it is believed that a drop below this value is physiologic, and that unless other changes occur along with it, a hemoglobin below the predetermined level does not constitute an anemia but rather a normal physiologic response.

The principal material consisted of 136 women who were followed during and after pregnancy. The hemoglobin, red cells, hematocrit, and mean corpuscular hemoglobin concentration were consistently lower than that of the control group even in the first trimester of pregnancy. Following this there was a continued decrease in the hemoglobin, red cells, and hematocrit values up to the last trimester when they all remained even, except the red count which increases. On the other hand, the serum iron level is normal during the first trimester and then begins to decrease. During the last trimester, all of the blood characteristics studied by the author showed means which were definitely lower than his control group. In an effort to explain the findings of hypochromia, which persists throughout the entire pregnancy, and the presence of microcytosis during the last 8 weeks of pregnancy, he postulates that hemodilution could account for the initial decrease and some deficiency in iron during the last 2 months of pregnancy. This is substantiated by an increased level of serum iron in the first portion of pregnancy with a decrease during the last 2 months. He was unable to find any variations because of economic status, age, or number of previous pregnancies. As expected, his studies on these blood values postpartum were directly related to the amount of bleeding during the intrapartum period. The greater the amount of hemorrhage, the lower were all the blood characteristics except the corpuscular value. The blood characteristics were stabilized between 1 and 6 weeks postpartum. The rather rapid increase of the blood characteristics following delivery suggests the mechanism of hemodilution. Again, however, the hypochromia may persist longer, and reflect the slow synthesis of hemoglobin.

A large percentage of patients, who were followed at a later date, showed persistent hypochromia until as long as 6 months postpartum.

The effect of the administration of iron on these lower blood values was studied and it was found that patients who had received a sufficiently prolonged and intensive dosage of iron, particularly in the latter part of pregnancy, had higher blood values, almost comparable to those in the nonpregnant individual. JAMES F. DONNELLY, M.D.

Endometriosis and Pregnancy. H. HUDNALL WARE, JR. *Am. J. Obst.*, 1950, 59: 715.

Thirteen cases in which pregnancy occurred in women with endometriosis are presented. In 12 of these, pregnancy occurred after conservative surgical procedures. In the remaining case, endometriosis without symptoms was observed at the time of cesarean section.

Three of the patients were between 22 and 25 years of age at the time of operation, and they later had 4 babies. Four patients between 26 and 30 years of age later had 6 babies. Three patients were between 31 and 35 years of age and had 3 babies. Two patients who were between 36 and 40 years of age later became pregnant but had early abortions.

In the 12 patients operated upon for endometriosis per se, the essential complaints were those of sterility, dysmenorrhea, and pelvic pain. The findings were those of fixed retroverted uterus with a palpable adnexal mass.

Surgery consisted of resection of the ovarian cysts, separation of the adhesions, and uterine suspension.

Only 2 of the patients have had any recurrence of symptoms. All are private patients and have been observed personally from several months to 18 years.

The prevalence of endometriosis in women of child-bearing age is now a recognized fact. Conservative surgery with preservation of the child-bearing function in these women and in those without children is recommended whenever possible.

JOHN R. WOLFF, M.D.

Pregnancy and Diabetes. WILLIAM P. GIVEN, R. GORDON DOUGLAS, and EDWARD TOLSTOI. *Am. J. Obst.*, 1950, 59: 729.

A review of 106 patients with 131 pregnancies complicated by diabetes is presented. The pregnancy of 75 per cent of these patients ended after 36 weeks.

The diabetes was treated by the clinical technique. There was no constant diminution of insulin requirements observed during pregnancy. Weight gain was not excessive. Toxemia was present in 46 per cent of the pregnancies, ketoacidosis in 16.8 per cent. There is no evidence that hyperglycemia is a contributory factor to the large infant, the greater incidence of toxemia, the episodes of ketoacidosis, and infant mortality. The pregnant diabetic requires rigid supervision by both obstetrician and internist, and immediate hospitalization is advised for acidosis, infection, and toxemia. Routine hospitalization at the thirty-fourth week for complete evaluation and decision as to the time and mode of delivery is recommended.

Labor was prolonged in 26 per cent of the primigravid patients and in 1.3 per cent of the multigravid patients. The incidence of forceps delivery was 10 per cent and of cesarean section 9.9 per cent. The sections were performed for obstetrical indications.

The maternal mortality was 1.5 per cent, represented by 2 patients in neither of whom was the diabetes the initiating cause of death. The maternal morbidity was 17 per cent.

The infant mortality rate was 21.4 per cent, and the total fetal loss was 30 per cent (including abortion, immature infant deaths, and ectopic pregnancy). Thirty per cent of the infants weighed over 4,000 gm. The severity of the diabetes did not affect the infant mortality. Toxemia, ketoacidosis, and the excessive size of the infant were the factors most often associated with infant death.

Intrauterine death of the fetus is most often associated with toxemia and ketoacidosis. Premature delivery for the patients with toxemia and those subject to ketoacidosis is recommended. Labor should be started by induction and vaginal delivery should be performed when possible. Should induction fail or labor become desultory and prolonged, cesarean section is advised. Water retention in the infant, as evidenced by a halo sign on roentgenography, is an indication for immediate delivery, provided the infant is alive. Recent advances in pediatric care have reduced the neonatal mortality, and infant survival is possible even when delivery is effected as early as the thirty-second week. The infants were routinely sent to the pediatric premature nursery where incubation, oxygen, suction, and dehydration formed the initial regimen of treatment.

The excessive-sized infant presents a special problem in that accurate estimation of the weight of such infants is subject to more than the usual error. The tendency to underestimate the weight of these infants may be influenced further by edema of the anterior abdominal wall and an unknown amount of amniotic fluid. Impaction of the shoulders is a major complication in delivery. Cesarean section is recommended for infants estimated to weigh more than 4,500 gm.

Hospitalization and premature delivery in the complicated case would reduce the infant mortality materially.

JOHN R. WOLFF, M.D.

Face and Brow Presentation. The Experience of the Johns Hopkins Hospital, 1896 to 1948. L. M. HELLMAN, JOHN W. W. EPPERSON, and FRANK CONNALLY. *Am. J. Obst.*, 1950, 59: 831.

The approach to the extended position of the fetal head should, in the main, be conservative as the great majority of cases will result in spontaneous or easy forceps delivery with a relatively low infant mortality. All of the patients with this condition should be meticulously studied from the standpoint of pelvic contraction, and x-ray pelvimetry should be performed on all of them when feasible. If pelvic contraction exists, cesarean section should be performed in view of the extremely high fetal mortality when this position is associated with a contracted pelvis. Version may still have some small place in the treatment of face and brow presentation, if the membranes have not been too long ruptured and the pelvis is normal. It is contraindicated in instances of contracted pelvis. Attempts at conversion may be of some worth, although in this series only 50 per cent of the attempts were successful. The concern exhibited by some authorities in regard to the fetal and maternal outcome in mentum posterior is not borne out in this series. Although 30 per cent of the face presentations fell under this group, spontaneous delivery occurred in half of them. Even in the others, in which more difficult types of delivery were resorted to, the infant mortality was not unduly high and there were no maternal difficulties.

CHARLES BARON, M.D.

LABOR AND ITS COMPLICATIONS

What Influence Has the Inherited Shape of the Skull on the Course of Labor? (Welchen Einfluss hat die ererbte Form des Schaedels auf den Geburtsverlauf?) E. PHILIPP. *Geburtsh. & Frauenh.*, 1950, 10: 176.

In the course of years the author has been observing hundreds of children born by cesarean section and has noted that there are actually certain distinctions to be observed in the shape of the head. In order to demonstrate these differences he has had the last 28 children delivered by cesarean section photographed to show the shape of the head in profile.

The first set of illustrations showed the profile of 7 infants who were delivered by section before the bag

of waters had ruptured. These infants had presented themselves by the head. Four of these were plainly of the long headed (dolicocephalus) type and 2 of the round headed (trochocephalus) form. The profile of the remaining child showed a transition form from the short-headed (brachycephalus) to the high short-headed (oxycephalus) type.

The second set of illustrations exhibited the profile contour of the heads of 11 children who were delivered by cesarean section after rupture of the bag of waters had occurred. The periods elapsed since the rupture ranged from 15 minutes to 10 days; however, in no case had the head of the fetus become fixed in the maternal pelvis, and an artificial configuration produced by the forces of labor could also be excluded in these cases. Five of these heads were dolichocephalic and 4 were trochocephalic. One of the remaining heads was also dolichocephalic; however, this was in a case of face presentation in a mildly contracted pelvis and the head had been subjected to the pressure of the inlet for 2 hours before the child was removed by section.

In the third set of illustrations are reproduced the photographic profiles of the heads of 10 children in pelvic presentations. In these the mother's pelvis could never have exerted any modeling effect on the heads of these children before they were removed by section. Nine of these children had the typical round head, or trochocephalic shape. The remaining head was of the so-called navicular shape. This conformation was undoubtedly the result of pressure on the head by the fundus of the uterus in the presence of a paucity of amniotic fluid. In this material the typical dolichocephalic head was absent.

The fourth illustration presents the head profiles of a pair of twins. The girl twin was in pelvic presentation with a typical trochocephalic head, and the boy twin, in cephalic presentation with a typical dolichocephalic head. Of course, this was not a uniovular pair, each being contained in its own amniotic sac, and therefore the demonstration is not so convincing as it would be in the case of identical twins. Nevertheless, the author states that he has noted this same tendency in other cases of twins which were uniovular.

Martius states in his text book on obstetrics that the shape of the infant's head is the product of heredity and of environment. This the author concedes; however, he believes that this study shows that the environmental influence on the shape of the child's head plays a much more important role than that of heredity. JOHN W. BRENNAN, M.D.

Constriction Ring Dystocia. DAN PRYTZ. *Acta obst. gyn. scand.*, 1950, 29: 304.

Constriction ring dystocia is a rare but definite clinical entity. Fetal mortality is usually high because conservative management is usually necessary to prevent uterine rupture and other complications that increase dangers to the mother.

This is a case report of constriction ring dystocia in which forceps delivery was accomplished in a simple manner following relaxation of the ring, which was aided in this instance by the inhalation of amyl nitrite. The use of amyl nitrite inhalation is recommended in all such cases as a simple means of relaxing this abnormal muscular spasm—the constriction ring. JOHN R. WOLFF, M.D.

Curare as an Adjunct in the Conduct of Labor. A Preliminary Report on Its Use in 200 Cases. LEO J. HARTNETT and HAROLD J. FREIHEIT. *South. M. J.*, 1950, 43: 277.

Curare was used in 200 deliveries at the onset of the second stage of labor with the membranes ruptured. Twenty units of "intocostrin" or 1 c.c. of "metubine iodide" was given intravenously. If desired, half of the original dose was given within 3 minutes after the initial dosage. Perineal relaxation was satisfactory in 91 per cent of the cases and was more marked in multiparas than in primiparas.

Curare proved harmless to mothers and babies in the dosages herein described, and did not interfere with the forces of labor in the second or third stage. It proved to be a valuable adjunct to anesthesia and analgesia, and of value in operative obstetrics. The perineal muscles evidently are affected by divided intravenous doses of curare before undesirable side effects appear. Curare proved to be of questionable value in the first stage of labor.

GEORGE BLINICK, M.D.

A 20 Year Statistical Review of 454 Consecutive Cesarean Sections. CLYDE J. GEIGER and JOHN R. DURBURG. *Am. J. Obst.*, 1950, 59: 588.

Four hundred and fifty-four cesarean sections performed during two periods, from 1928 to 1937 and 1938 to 1947, are analyzed and compared. The incidence of cesarean section in the first 10 year period was 3.54 per cent as compared to 2.44 per cent in the second. The indications for cesarean section have remained about the same in both decades. There has been a definite trend to low cesarean section in the second 10 year period. Cesarean hysterectomy was employed more frequently in the second decade with no maternal mortality. The mortality rate was 3.30 per cent—5.70 per cent for the first period and 1.5 per cent for the second. There were no deaths due to postoperative infection in the second period, which is attributed to the more frequent use of cesarean hysterectomy and the utilization of antibiotics, chemotherapy, and the blood bank. The infant mortality rate was reduced from 10.6 per cent to 7.8 per cent. GEORGE BLINICK, M.D.

GENITOURINARY SURGERY

ADRENAL, KIDNEY, AND URETER

Adrenal Pheochromocytoma Without Hypertension (Phéochromocytome surrénalien sans hypertension). PAUL A. POLIQUIN and PIERRE DUPUIS. *Laval méd.*, 1949, 14: 1127.

The authors present a brief review of the embryology and histologic characteristics of the autonomous nervous system and discuss the symptomatology and anatomy of pheochromocytomas.

The great majority of these tumors are benign and unilateral. A large proportion of the bilateral ones are malignant. The benign tumors usually contain functioning tissue resembling the medulla of the adrenal gland and causing disturbances of circulation and metabolism (hypertension, hyperglycemia); the malignant ones are physiologically inactive.

Most of the pheochromocytomas are located at the adrenal medulla but they may occur also at other sites where there is chromaffine tissue. Cases are on record in which the tumor originated in the retroperitoneal space, in ganglia of the aorta and vena cava, in the thoracic sympathicus, in the sacrococcygeal gland, and in the rudimentary organ of Zuckerkandl.

The authors report the case of a woman, 52 years old, who developed a large mass in the left hypochondrium which simulated a kidney tumor. Surgery revealed a large retroperitoneal pheochromocytoma (18 by 14 by 9 cm.) which had displaced the kidney downward toward the pelvis. The greatest part of the tumor consisted of necrotic cells, only a small portion at the periphery showed living tissue.

The case is remarkable because the patient did not show any clinical symptoms of hypertension or metabolic disturbances.

WERNER M. SOLMITZ, M.D.

Experimental Contribution to the Study of Nephroangiography (Contributo sperimentale allo studio della nefroangiografia). VITTORIO SCRUFARI and MARIANO DALLA POZZA. *Urologia*, 1949, 16: 525.

The authors coined the term "nephroangiography" for a method introduced by them for the purpose of visualizing the renal arteries. This is accomplished by introducing a highly concentrated iodine compound into the lumbar portion of the aorta.

To study the histologic changes in the kidneys, the authors introduced the opaque medium into the aorta or the renal artery of rabbits after opening the peritoneal cavity. The kidneys were removed at various periods of time after the injection and were examined microscopically.

Degenerative processes in normal kidneys were most pronounced in the convoluted tubules because this part of the renal system excretes the opaque medium. The effect on the vascular system may be ascribed to the chemical action of iodine, the physical properties of a hypertonic solution, and the mechanical factors, namely, the puncture of the adventitia of the renal artery with the needle. Apparently only the toxic factor is of clinical importance. A certain degree of cortical ischemia may follow the injection in the presence of a manifest lesion of the kidneys.

If the amount of the opaque medium does not exceed 1 c.c. per kilogram of body weight, aortographic examination does not aggravate bilateral nephropathy with renal insufficiency.

JOSEPH K. NARAT, M.D.

The Problem of the Pyelorenal Ectasias. The Hydronephroses. Their Treatment (El problema de las ectasias pielorrenales. Las hidronefrosis. Su tratamiento.) LUIS A. SURRACO and JORGE LOCKHART. *An. Fac. med.*, Montev., 1949, 34: 1199.

From this discussion are excluded the ascending type of hydronephrotic ectasias, such as that form of hydronephrosis secondary to obstructive conditions at the mouth of the urethra or neck of the bladder. Treated apart are also the ectasias about the pyelorenal area secondary to a blocking of the urinary passages by such conditions as tumor, stone, and clots, in which the treatment is directed toward the block itself rather than toward the hydronephrosis as such.

These ectatic dilatations are also divided for purposes of treatment into those of congenital origin and those of the acquired type. The congenital types might, of course, be the result of the kinking of a ureter in a congenital nephroptosis; however, this would be extremely rare and the congenital hydronephroses are practically limited to an abnormal thickness of the musculature at the mouth of the ureter, that is, at the region where the renal pelvis joins the upper end of the ureter. This musculature forms a true sphincter and at this level consists of 3 layers, an inner circular muscle layer, a middle longitudinal layer, and outside this layer again, an external circular layer of muscle fibers.

Both the circular muscle layers of this pyeloureteral sphincter are, as a rule, hypertrophied in these congenital cases and the hypertrophic condition will extend for varying distances above the narrowest point (ostium) onto the infundibulum, or funnel-shaped lower end of the pelvis leading down to the ostium, and below the ostium for a distance of 1 or 2 cm. along the course of the upper end of the ureter. This portion of the upper end of the ureter immediately following the ostium is designated the isthmus.

In the congenital forms of hydronephrosis, therefore, especially in the cases with mild dilatation, it may be sufficient to simply evulse this sphincter, which the authors regard as more or less a corollary of the Rammstedt procedure for pyloric hypertrophy

and of the various methods of dilating other spastic sphincters. In this instance, however, the sphincter is not cut but simply dilated forcibly but gently by opening the renal pelvis and inserting a curved fine pliers or hemostat through the ostium and opening its blades. This method is naturally much more effective than the standard—rather timid—practice of introducing graduated sizes of olive-tipped probes. As a rule, in these cases the isthmus will also show this condition of spasm and will have to be dilated to the point where it widens out into the definitive ureteral canal. However, care will have to be exercised as the isthmus is sometimes rather friable (perhaps resulting from inflammatory changes) and may be easily perforated or ruptured.

For the larger hydronephrotic dilatations of the congenital cases and for the general type of acquired forms further operative procedures will be necessary.

In any type of hindrance to the urinary flow, inflammatory changes are likely to be present. Most frequently these changes will be encountered in the space between the external lamina propria of the ureteral musculature and the so-called vascular lamina of Ombrédanne. Between these two laminae the ureter lies loosely as in a bed or compartment filled with loose connective tissue and traversed by the vascular pedicle or mesoureter, and wherein the peristaltic contractions of the ureter can progress freely. If this compartment shows sclerotic changes enveloping the ureter, this organ must be freed without, however, interfering with its vascular supply. It is best in this freeing procedure to enter the compartment from the back and merely free the ureter sufficiently to permit of free peristaltic movement. This periureterorenal lamina of Ombrédanne extends much farther down along the course of the ureter than is generally indicated in text books of anatomy.

In the larger forms of hydronephrotic dilatations of the renal pelvis, in which more extensive procedures are indicated, the usual procedure is a plication of the hydronephrotic sac and drainage. The method of plication is shown in the appended illustration (Fig. 1). The drainage is performed by introducing a small rubber tube through the opening in the renal pelvic sac on a curved pliers and the end is brought out again through the kidney substance, entering in the summit of one of the calyces and emerging on the lateral surface of the kidney. The two ends of this tube are then fastened together with a safety pin, and drainage is permitted to go on for much longer than is customary, perhaps for several weeks and in some cases for months; in 1 instance it was continued for a year.

In the presence of nephroptosis a suspension operation may, of course, be indicated. It will hardly ever be necessary to sever any of the blood vessels to or from the kidney, although the supplementary blood vessels of anonymous character to the upper and lower renal poles may be sacrificed without danger as a rule. The hydronephrotic sac must, however, always be freed thoroughly from its cradled position among the forking branches of the hilar ves-

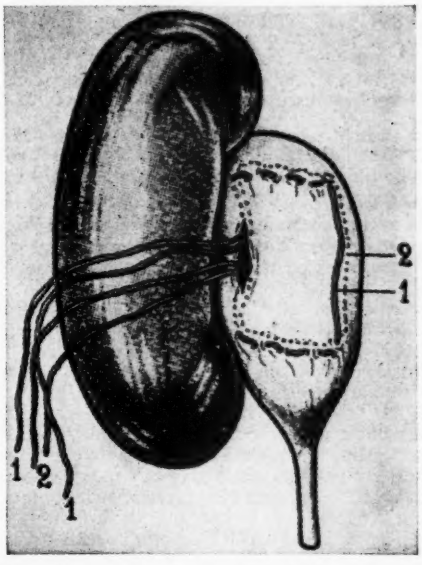


Fig. 1 (Surraco, Lockhart). Pyeloplastic. The sutures *1* and *2* describe the trajectory indicated on the anterior and posterior walls of the hydronephrotic sac emerging from the orifice of the pyelotomy.

sels, as otherwise it will not retract properly no matter how long the drainage proceeds.

The indications for each type of procedure are not fixed. As a rule, it is only when the viscus (as the authors express it) is held in the surgeon's hand that a final decision as to method and extent of operative procedure can be made. In the so-called small hydronephroses, laboratory procedures will not be of much help. The physician will have to depend upon the clinical picture (pain, pyuria, hematuria), which must furnish the indications. The authors do not pretend that the diagnosis in these cases is an easy matter. There will frequently be symptoms present in other organs in the vicinity or at a distance (stomach, gall bladder, esophagus), and such symptoms will have to be differentiated from the symptoms of the hydronephrotic process proper. This will be doubly difficult at times because the organs in the vicinity, or at a distance, will sometimes produce symptoms which may be referred to the pyeloureteral region, and such symptoms will have to be duly considered if any hope of relief for the patient is to be expected from operative interference.

Nephrectomy is never indicated in the small hydronephroses and can be considered in the larger forms only when the other kidney shows satisfactory functioning. The general tenor of the treatment must always be conservative.

The views here expressed, which may sound revolutionary to many physicians, must be considered as

the mature pronouncements of men whose many previous publications concerned with the problems of hydronephrosis and those of nearly related subjects prove a long period of preoccupation with the matters here discussed. JOHN W. BRENNAN, M.D.

The Pathogenesis of Tuberculosis of the Kidney. W. A. MOONEN. *Arch. chir. Neerl.*, 1949, 1: 296.

The theory of hematogenic origin of renal tuberculosis has the most adherents at this time. Opposition to the acceptance of this concept in the surgical type has been due to the following reasoning: (1) surgical renal tuberculosis is in most cases unilateral; (2) the process starts in the medulla; and (3) hematogenically induced tuberculosis in animals has invariably shown all the qualities of the miliary type, i.e., it has been bilateral and cortical.

In support of the hematogenic theory, the work of Medlar is reviewed. This showed clearly that surgical tuberculosis of the kidney is preceded by a stage of hematogenic bilateral cortical tuberculosis (the preclinical stage). Examinations of the "sound" kidneys of patients who had clearly shown unilateral surgical tuberculosis of the kidney revealed numerous cortical microscopic foci tending to heal, or healed.

This preclinical renal tuberculosis occurs probably in a very large percentage of cases of lung tuberculosis and might be demonstrated by systematic and repeated cultures from the urine. Since this is a manifestation of hematogenic dissemination, lesions of preclinical significance may also be expected to exist in other organs. The frequent concurrence of orthopedic tuberculosis makes it likely that serial sections of the medulla ossium would reveal tubercles.

The origin of the initial focus of a surgical type in the medulla is explained by the implantation of tubercle bacilli excreted by the cortical focus onto an embolus of shed cells or bacteria in the tubules. Animal experiments of Coulaud have shown initial renal irregularities in the cortex which in unfavorable situations reach the medulla by the endotubular route. Destruction and caseation of the parenchyma with pyelographic irregularities, positive smear, and evidence of impaired renal function follow. Those authors who estimate that 10 per cent of the tuberculosis of the kidneys is bilateral have this type of change in mind. Those who state that 100 per cent of the cases are bilateral are considering the preclinical group with positive culture studies and no clinical changes.

The controversy regarding the primary site in the genitalia is discussed. The author believes that as part of the generalized hematogenic dissemination, minute preclinical foci may arise in the epididymis, prostate, and seminal vesicles. In most of the cases seen, the primary focus seems to have been in the epididymis, but isolated involvement of the prostate has been noted. In conclusion, the pathogenesis of genital tuberculosis cannot be conceived to be apart from renal tuberculosis. The two clinical pictures are manifestations of one disease—urogenital tuberculosis. ALLAN K. SWERSIE, M.D.

Suppurating Solitary Cyst of the Kidney (Cisti solitaria suppurata del rene). PASQUALE FICARA. *Arch. ital. urol.*, 1950, 24: 56.

Since 1940 Ficara has encountered 3 cases of solitary serous cyst of the kidney among 187 renal operations. The first 2 cases presented nothing of particular importance, but in the third case the cyst, which occupied the middle portion of the anterior aspect of the right kidney in the vicinity of the hilus, was complicated by suppuration of its cavity and by chronic interstitial nephritis. Nephrectomy was performed because of hemorrhage during the intervention, and histopathologic examination revealed a tendency toward the formation of small secondary cysts in the renal parenchyma.

An interesting fact in this case was the suppuration of the cyst as inflammation of renal cysts is rare, and perforation of the cysts into the renal pelvis is extremely rare. Suppuration may occur through the passage of bacteria from the pelvis to the cyst by the lymphatic route or through the canalicular route by infection of hematogenous origin. In the present case both possibilities were acceptable.

The urinary findings, especially the numerous leucocytes and some granular casts, would lead one to believe that, in addition to the endocystic suppuration, there was also inflammation of the renal pelvis and secondary infection of the parenchyma. However, pyelography did not demonstrate any direct communication between the cystic and pelvic cavities and excluded the possibility that the pus in the urine depended on perforation of the cyst into the renal pelvis. During descending urography the cystic cavity became opaque, demonstrating that numerous uriniferous canalicules opened into it and suggesting that the bacteria had followed the same route after having reached the kidney by way of the blood steam. Since the cystic cavity became completely free of contrast substance, it is admissible to think that distally, also, the cyst communicated with the collecting tubules of the kidney and through these with the pelvis. Therefore, the author is convinced that the presence of pus in the urine was due in part to elimination of the cystic contents through the excretory tubules of the kidney and in part to the concomitant primary or secondary infection of the renal pelvis.

The second interesting point of this case was that the cystic cavity, which was made visible by urography, could not be demonstrated by ascending pyelography, which showed only a moderate dilatation of the upper calyx and a slight enlargement of the space between the upper and intermediate calyces. These roentgen data and the acute course of the disorder which was benefited by penicillin facilitated the diagnosis of suppurative solitary cyst of the right kidney.

In most cases the intervention may be conservative: renal resection when the cyst is at the upper or lower pole, or resection of the capsule when the cyst is in the median part of the kidney or on its convex border. The bottom of the cyst is then

destroyed by the thermocautery or by diathermocoagulation. If the cyst protrudes much, an attempt may be made to remove it by dissection. Nephrectomy is rarely necessary but is justifiable in cases of marked renal atrophy, when there is abundant bleeding after removal of the cyst (hematic cyst), or when hilar implantation of the cyst makes hemostasis difficult. RICHARD KEMEL, M.D.

Replacement Lipomatosis and Its Simulation of Renal Tumors: A Report of 2 Cases. WAYNE A. SIMRIL and D. K. ROSE. *J. Urol.*, Balt., 1950. 63:588.

Replacement lipomatosis is a condition in which areas of fat replace renal parenchyma destroyed by atrophic or necrotic processes. Although these areas do not invade or become malignant, they seem to encroach on the calyces or pelvis of the kidney and thus frequently result in a filling defect on pyelography. Nonencapsulated replacement lipomatosis is to be distinguished from the encapsulated perirenal and intrarenal lipomas.

The process of replacement lipomatosis may be either inflammatory or noninflammatory. In the majority of cases inflammation is present but this condition is seen in some noninflammatory degenerative conditions such as arteriosclerosis and amyloidosis. The disease is almost always unilateral. Roth and Davidson pointed out that in the presence of chronic renal infection, calculi, poor function on the affected side, and a filling defect in the pyelographic study, a presumptive diagnosis of replacement lipomatosis should be entertained.

The authors report 2 cases, in one of which the preoperative diagnosis of replacement lipomatosis was suggested. Both cases were in elderly individuals who had a long history of unilateral flank pain. Both had evidence of urinary tract infection. Pyelography demonstrated filling defects indistinguishable from those caused by tumors. Nephrectomy was performed in both instances and revealed, in addition to acute and chronic pyelonephritis, replacement of renal parenchyma by fatty tissue. It was this fatty tissue which caused the filling defect evident on pyelography.

The authors emphasize the fact that persistent filling defects in the kidney should be regarded as tumor. To further emphasize this fact they present a pyelogram of an epidermoid carcinoma of the renal pelvis in which the filling defect is not nearly as apparent as in the cases of replacement lipomatosis.

JOHN T. GRAYHACK, M.D.

Dorsolumbar Approach to the Kidney and Adrenal Gland with Osteoplastic Flap. GEORGE NAGAMATSU. *J. Urol.*, Balt., 1950, 63: 569.

It is generally conceded that in many instances the routine lumbar exposure of the kidney is inadequate. The proximity of the kidney to the back makes the posterior approach seem logical in some cases, if the difficulty caused by the presence of the rib cage could be circumvented.

In the operation described by the author an incision is made just medial to the angle of the ribs extending from the superior border of the twelfth rib to the ninth interspace. The horizontal limb of the incision is then made parallel to the twelfth rib. The lower skin flap is retracted downward, and the superior lumbar triangle is identified. The anterior margin of the latissimus dorsi and the serratus posticus inferior muscle are freed. Next the tendinous slips of the sacrospinalis are removed from the lower ribs. About 2.5 cm. of rib are resected from the tenth, eleventh, and twelfth ribs just medial to the angle. The lateral arcuate ligament of the diaphragm is freed inferiorly, the lumbocostal ligaments are divided below the twelfth rib, and the external arcuate ligament of the diaphragm is divided. No attempt to dissect the pleura is made but the whole mobile flap thus developed can now be swung upward. If a rent is made in the pleura at this time, it is packed and later sutured. The kidney is palpated and the lumbar portion of the incision extended as necessitated by the position of the kidney. In extending the incision, the linea semilunaris should be left intact if possible, and the incision should not extend upward beyond the level of the twelfth rib. A Balfour type of self-retaining retractor is placed at the angle of the ribs, and the kidney is exposed extrapleurally and extraperitoneally.

In closing the wound the structures are reapproximated anatomically. Intracaine-in-oil (4–5 c.c.) is injected into the periosteum and surrounding structures at the proximal cut end of each rib. If the pleura has been entered, the edges of the rent are caught in a purse-string suture. After removal of the air from the pleural cavity by positive pressure anesthesia and a catheter inserted through the rent, the catheter is removed and the suture tied.

Postoperatively, the patients are encouraged to cough, breathe deeply, and move about. No serious instances of atelectasis or other complications have been noted.

The author recommends the extrapleural retroperitoneal exposure for cases in which adequate exposure is difficult to obtain by ordinary methods. He suggests that the added time needed to perform the first step of this procedure is more than compensated for by the relative ease of removing kidneys and adrenal glands that would be very difficult to handle through the usual lumbar incision. This approach is advocated only as a primary procedure and not as an expedient to an inadequate lumbar incision. The author advises its use in some kidney tumors, adrenal tumors, high-fixed kidneys, and secondary nephrectomies.

JOHN T. GRAYHACK, M.D.

Suture of the Fibrous Capsule after Nephrotomies (Sutura della capsula fibrosa nella nefrotomia). LODOVICO GURGIAN-CECCONI. *Urologia*, 1949, 16: 537.

Nephrotomy is fraught with the danger of a postoperative hemorrhage which may be early or late.

Hemostasis may be difficult to accomplish because of fragility of the renal tissue, and early postoperative bleeding is the result. Hemostasis obtained by various methods may lead to alterations of the renal parenchyma, which in turn may be the cause of late hemorrhage, which usually occurs from 8 to 10 days after the operation.

Various suggestions have been offered to prevent such hemorrhages; for instance, introduction into the split kidney of particles of fat, muscle tissue, omentum, fibrin foam, gelatin sponge, or oxidized cellulose; suture of the capsule only and not of the renal tissue; and the employment of electrocoagulation.

The author performed bilateral nephrotomy in a horizontal or vertical direction on rabbits and sutured only the capsule, without a previous attempt to separate it from the kidneys. The histologic examination showed the formation of connective tissue in the region of the nephrotomy, with minimal alterations of the glomeruli and tubuli, confined to the line of the incision. JOSEPH K. NARAT, M.D.

Behavior of the Contralateral Kidney in Renal Decapsulation (Sul comportamento del rene adelfo al rene decapsulato). ERNESTO COMINELLI. *Arch. ital. urol.*, 1950, 24: 30.

The author has used the following technique in 9 adult male rabbits. First, he collected vesical urine by catheter and analyzed it carefully. Then, after depilation, he made an incision on one side parallel to the external border of the quadratus lumborum and resected the ureter paraperitoneally as low as possible. He abandoned the distal stump, exteriorized the proximal stump, which he fixed to the skin, and closed the wound in two layers. For 3 days he collected vesical urine by catheter and analyzed it. On the fourth day he decapsulated the kidney with the neostomized ureter and, beginning on this day, he examined the vesical urine every day until the animal was killed. Three animals were killed 6 days after the first operation and 48 hours after decapsulation, another group of 3 were killed 8 days after the first operation and 5 days after decapsulation, and the remaining 3 animals were killed 11 days after the first operation and 8 days after decapsulation.

In the first 3 days of the experiment the urines of the 9 animals showed no true differences in urea concentration. During the first 24 hours after decapsulation, the urea concentration of the contralateral kidney was notably increased, and the increase continued until the fifth to sixth day of the experiment, but underwent a critical phase on the sixth to seventh day when the urea level was decidedly lower than before the experiment. The chlorides immediately after decapsulation decreased rapidly in the urines; this phenomenon was constant in all animals and was all the more interesting because in 6 of them the first operation had caused a rapid concentration of chlorides.

Histologic examination revealed in the contralateral kidney during the first 48 hours a notable increase of the capsular spaces and a dilatation of the contorted tubules which in many points were filled with hemorrhagic exudate, so that the entire cortical substance was markedly hyperemic, especially in its peripheral portion. These changes progressed during the subsequent days instead of regressing. Beyond the fifth day there were only a few red cells free in the lumen of the canalicules, while the swelling of the malpighian glomeruli or the tubular dilatation persisted. It would thus seem that after this time the renal changes become stabilized and the conditions for more active excretory function are created. There seemed to be no modification in the excretory part of the parenchyma, which suggested that the nerve fibers of this region of the kidney have no connection with the corticocapsular innervation. These findings mean that the capsulocapsular reflex does not occur through the branches of the renal plexus, but rather through a sensitive vasomotor capsulocapsular reflex. RICHARD KEMEL, M.D.

Obstruction of the Urinary Outflow from the Remaining Kidney as the Cause of Late Mortality after Nephrectomy for Tuberculosis of the Kidney. W. A. MOONEN. *Arch. chir. Neerl.*, 1949, 1: 303.

Deaths following nephrectomy for tuberculosis which occur between the sixth month and twelfth year after operation fall into a "late mortality" category. In the early postoperative months, mortality is frequently classified as operative in origin, but after 12 years, death from urogenital tuberculosis is very rare. The studies on late mortality are based on 118 surgically treated patients who could be followed up. Of these, 16 belonged in this group.

The causes of death during this period, in order of frequency, were (1) renal insufficiency, (2) tuberculosis of the lung, and (3) miliary tuberculosis. Interest is centered about factors that cause insufficiency in the remaining kidney with the hope of anticipating this development and undertaking prophylactic measures. Thirteen cases of renal insufficiency with death were closely studied to determine the changes responsible for the failure. In order of frequency, the final changes are believed to be (1) hydronephrosis due to stricture of the lower part of the ureter, (2) urosepsis, and (3) tuberculous re-infection.

Development of hydronephrosis in the remaining kidney because of low ureteral obstruction occurs with marked frequency and is demonstrated in case presentations by autopsy findings and x-ray data when available. In further demonstration of such development when such evidence is not to be had, recourse is made to early studies of the cases, including the prenephrectomy information. Inferences are reached that certain clinical data and observations imply present or future obstructive changes in the "healthy" kidney. For example, difficulty in catheterization of ureteral orifices, continuous pain in the region of the kidney rather than complaints of ordinary cystitis as the dominating subjective symptom, and findings of continuous

ureteral flow showing loss of peristaltic action are premonitory indications of hydronephrosis.

When hydronephrotic changes occur in a tuberculous surgical kidney, the prognosis is poor since there is a marked regularity in the development of the same obstructive process in the lower ureter on the "sound" side. Such obstructive development should be anticipated also when there are the aforementioned premonitory symptoms of hydronephrosis. Early operation before there is extensive bladder involvement with cicatricial changes producing low ureteral stricture should be the first objective. It is imperative regularly to examine patients who have undergone nephrectomy for tuberculosis by urography. When obstruction is demonstrated, early surgical restoration of the urinary outflow by nephrostomy or ureterostomy may prolong life and comfort. In favorable cases, when the urine culture is negative and bladder tuberculosis is cured, the ureter may be severed above the stenosis and reimplanted in the bladder. Illustrative cases are presented. ALLAN K. SWERSIE, M.D.

Subcutaneous Rupture of the Ureter. R. WILENIUS. *Ann. chir. gyn. fenn.*, 1950, 39: 1.

By subcutaneous rupture of the ureter, the author means that the rupture has been accomplished without an open wound or incision. A complete review of the literature is given with an excellent bibliography of both clinical and experimental work.

The author reports 4 cases of his own in which subcutaneous rupture of the ureter occurred. The patients were from 2 to 11 years of age, and the rupture was traumatic in origin. One patient was run over by a motor car and 1 by a lorry, 1 was jammed under a horse cart which overturned, and the last 1 was knocked over by a motor car and thrown into a ditch. These 4 cases are abstracted in the original article.

In a discussion of the diagnosis the author mentioned shock as a frequent finding. Hematuria, however, is relatively uncommon. In cases of extraperitoneal rupture, symptoms due to urinary infiltration and infection may develop slowly, and several days or weeks may pass before surgical intervention is undertaken. The author advised excretory urography and, if necessary, retrograde pyelography to establish the diagnosis. The most acceptable treatment is suture of the ruptured ends of the ureter over a ureteral catheter.

The last half of the article deals with a consideration of the mechanism of rupture of the ureter. A survey of the literature on this subject is given, and then the author describes his experimental work on the subject. His investigative work was done on 19 cadavers (38 ureters). An attempt was made to crush the ureters by rolling a heavy wheel across the abdomen at different levels and also by blows with the end of a pole against the ureter over the transverse processes of the lumbar vertebrae. In the case of the wheel, the ureteral lesions in most cases were partial and were generally caused by the wheel's crushing the ureter against the second, third, or fifth lumbar vertebra. By a blow applied directly, the ureter could be crushed against the transverse processes of the second and third lumbar vertebrae. Also, indirect total ruptures due to traction were produced in exceptional cases. The ureter is most susceptible to rupture in the vicinity of the isthmus and in the region of the opening into the bladder. Hydraulic factors are of almost no significance in the production of rupture of a normal ureter.

JOHN L. EMMETT, M.D.

GENITAL ORGANS

Nonspecific Granulomatous Prostatitis. W. ST. C. SYMMERS. *Brit. J. Urol.*, 1950, 22: 6.

The etiology of nonspecific granulomatous prostatitis appears to be an unusually severe reaction to the presence of retained secretion in ducts or acini, and to its escape into the stroma. In at least some cases, the history suggests a nonspecific infection as a factor in destroying the duct lining and permitting the escape of secretion into the surrounding tissue.

Three cases are given as examples of both the focal and diffuse types of granulomatous prostatitis, together with several illustrative photomicrographs. The author lists the etiologic factors in acute, chronic, and nonspecific granulomatous prostatitis.

The pathology of focal nonspecific prostatitis is discussed. The commonest type has localized infiltrations by inflammatory cells, due to duct infection and lining destruction. The type of cell in the exudate depends on the chronicity and the organism. Histiocytes do not participate in the reaction to a degree greater than in comparable inflammatory reactions elsewhere; metamorphosis to epithelioid cell types does not occur.

The second variety is a granulomatous one with large mononuclear cells predominating. They occasionally develop around the corpora amylacea, which develop following partial or complete destruction of the acinar lining due to infection or pressure of concretions. The concretions gradually disappear when granulomas form around them, and all stages of disappearance can be seen in the different inflammatory foci. The effect of lipoid substances present in the secretions may also play a role in the development of the granuloma. It may be that where no corpora amylacea are present, the lipoid material may play the major role, especially sphingomyelin (Tanner and McDonald, 1943). Histologically there is epithelioid cell proliferation, lymphocytes and plasma cells, and usually some multinucleated foreign body giant cells. Occasionally a small area of necrosis may develop at the center of the lesions.

The diffuse nonspecific granulomatous prostatitis is identical with the focal variety, being more extensive. The histologic appearances are essentially the same. Variations as to the predominant cell type may appear. In one type plasma cells may be so numerous that it is reminiscent of so-called plasma

cell mastitis. Similarly the lesion resembles chronic sclerosing granulomatous thyroiditis (Riedel's disease).

The diffuse type of prostatitis may be similar to the lesions of tuberculosis and should be differentiated. Similarly sarcoma, though rare, must be ruled out. In the sclerotic type, particularly where plasma cells are numerous and blood vessels show mural thickening, syphilis may be suspected. Careful histologic examination is advised.

NATHAN ROSENBLOOM, M.D.

Cause of Death of Patients with Hypertrophy of the Prostate Gland (Le cause di morte nei prostatici). GIORGIO RONCAGLI. *Urologia*, 1949, 16: 545.

Of 558 patients with hypertrophy of the prostate gland, 476 were operated upon, and 49 of them, or 10.7 per cent, succumbed to the operation. Cystotomy was performed on 279 patients, with a 7.5 per cent mortality. Suprapubic prostatectomy in two stages was performed on 179 patients, with a mortality of 13.9 per cent. The same operation in one stage was performed on 18 patients, with a mortality of 16.6 per cent.

Post-mortem examinations in 60 cases showed cystopyelitis to be present in 21.6 per cent of cases in this series, cystitis in 20 per cent of cases, pyonephrosis also in 20 per cent, and other complications in a lesser number of cases.

From a study of the reported series, the author concludes that urinary infections, especially those of the upper portion of the tract, are chiefly responsible for the fatal outcome after prostatectomies.

Administration of sulfonamides did not markedly depress the postoperative mortality, while the number of fatalities has dropped sharply since the introduction of penicillin.

The author stresses the necessity of a careful preoperative study of the morphology and the function of the urinary tract by means of the dilution and concentration test, the phenolsulfonphthalein test, determination of the nitrogen contents of the blood, intravenous urography, and chromocystoscopy.

JOSEPH K. NARAT, M.D.

Cryptorchidism and Ectopy; Concerning a Case of Perineal Ectopy of the Left Testis (Criptorchidia ed ectopia; a proposito di un caso di ectopia perineale del testicolo sinistro). F. GAROFALO. *Arch. ital. urol.*, 1950, 24: 3.

The author had examined this patient 10 years previously when he was 9 years old and had then recommended operation, which was refused by the parents. At the present examination the perineum showed a small mass in the triangle formed by the anus, the bulb, and the left ischiatic tuberosity; by its form, consistency, and sensitivity this mass recalled the characteristics of a testis, and it was so mobile under the intact skin that it could be pushed posteriorly to the anus and anteriorly to the external inguinal ring. Palpation gave the impression of a trophic organ of normal volume, which continued upward with a thinned, long cord issuing from the inguinal ring which was smaller than the right one. The arrangement of the scrotal folds indicated a rudiment of left hemiscrotum; the right testis, epididymis and cord, the prostate, and the seminal vesicles were normal.

Under local anesthesia, the author made a vertical incision from the external inguinal ring to two fingerbreadths from the left ischiatic tuberosity on the paramedian line. He isolated the spermatic cord and by pulling on it and pressing on the perineum, moved the testis upward; he resected the bottom of the vaginal tunic which was large and from which issued a fibrous cord surrounded by veins that entered the cellular tissue of the perineum; he closed with catgut the cleavage plane of the testis and fixed the bottom of the vaginal tunic in the scrotal sac that had been prepared by the usual digital maneuver; finally, he reduced the size of the neck of the sac with a few stitches and closed the soft tissues in two layers. The testis was well developed. The postoperative course was normal.

According to Alyea, 2 per 1,000 of young subjects have cryptorchidism, while the statistics of the American draft during the last war showed that 3.1 per 1,000 of the recruits presented this anomaly which was more common in the northern states, inhabited by whites, than in the southern states, more inhabited by negroes. The varieties of congenital ectopy are the perineal, pubopenian, crural, femoral, and crossed.

The author discusses the genesis of testicular ectopy, confronting the mechanical theories of Hunter and Lockwood with the biodynamic theory of Ruffini who distinguishes three elementary morphogenetic processes: (1) ameboidism, (2) secretion, and (3) multiplication of the cells. This concept of Ruffini applied to the descent of the testis offers the most convincing explanation of the genesis of cryptorchidism and ectopy. The processes of Ruffini intervene in the formation of the primary organs and the forms of the body, and are regulated by hormonal stimuli or formative impulses; hence, disturbances of internal secretions interfere with the interaction of these processes, and result in the appearance of anomalies. RICHARD KEMEL, M.D.

MISCELLANEOUS

Evaluation of Sterility Problems of the Male. EDMOND J. FARRIS. *J. Urol.*, Balt., 1950, 63: 748.

After studying males in 3 categories, (1) those whose wives conceived without difficulty, (2) those whose wives conceived with difficulty, and (3) those whose wives failed to conceive, a new classification of patients was evolved, one which was based solely on the total number of motile spermatozoa in the ejaculate.

Four classes of males resulted: (1) those with high fertility—with at least 185 million spermatozoa, (2) those with relative fertility—with from 80 to 185 million, (3) those with subfertility—with a total be-

low 80 million, and (4) those who were sterile—in whom no spermatozoa were found.

The technique of the new method for study is outlined as well as the accepted minimal standards for a good prognosis. The latter include 4 c.c. of total volume, 87 per cent of oval forms, and 44 per cent of motile forms, or 51 million per cubic centimeter. The total or absolute motility average was 209 million. Only 3 per cent of the patients that fell below these standards were able to impregnate their wives.

The spermatozoon counts on men in the high fertility group varied very little but the counts in the lower categories varied from subfertile to highly fertile in as many as 14 per cent of the individuals, when more than one determination was made.

Clinical evaluation of any unsuccessful couple, according to the author's plan, includes counting the number of active spermatozoa, hysterography to evaluate the wife's tubes, and calculation of the probable date of ovulation. A group of 100 sterile couples who succeeded in having children is presented in detail. Only 40 per cent of the husbands had high fertility.

On the basis of these 100 successes and other clinical observations, it is suggested that highly fertile husbands concentrate coitus on the precise day of ovulation or have intercourse on the eleventh, twelfth, and thirteenth days of the cycle. Those that belong in the relatively fertile group should have coitus twice on the day of ovulation, either within 8 hours or late in the evening and early in the morning. The subfertile type is advised to have coitus twice within 8 hours on the day of ovulation.

Special studies are reported regarding the effects of the frequency of emission, ageing of the sperm, and physical fatigue. Five days of abstinence permit the greatest concentration of active spermatozoa. The fertilizing power of the spermatozoa seemed to be lost in 12 to 24 hours. Extreme physical exertion had no deleterious effect on the sperm picture.

ORMOND S. CULP, M.D.

Functional Evolution of the Neurogenic Bladder in Paraplegic Patients. ERIC P. STONE. *J. Urol.*, Balt., 1950, 63: 673.

The progress of the neurogenic bladders in 272 quadriplegic and paraplegic patients at Cushing Veterans Administration Hospital formed the basis for this report.

For the final result to be considered "satisfactory," the author insisted that the patient have control of the time of voiding, have no incontinence, develop a bladder capacity of from 210 to 300 c.c., and have not more than 60 c.c. of residual urine.

Recovery was constantly threatened by a number of potential complications. In these patients, 271 episodes took place that either caused regression or halted progress. Mass spasms were the worst neurogenic disturbance during this period. However, the greatest problems proved to be of urinary tract origin.

Urinary complications included hypertrophy of the vesical neck, incontinence, spasm of the external sphincter, aneurysm of the bladder wall, contracted bladder, ureteral reflux, calculi, urethral fistulas and diverticula, infection, and a few less common conditions. Each of these pathologic entities is considered in some detail.

The author offers a plan for study and follow-up as well as a complete outline for the management of paraplegic bladders, including definitive treatment of the complications.

Fifty per cent of the total number of patients had satisfactory results when last evaluated.

ORMOND S. CULP, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS

CONDITIONS OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Infantile Cortical Hyperostosis. Review of the Literature and Report of 5 Cases. MARY S. SHERMAN and DAVID T. HELLYER. *Am. J. Roentg.*, 1950, 63: 212.

This excellent article deals with a disorder of the bones of infants, which is either a new syndrome or one which has been overlooked until recently. Only 22 clear-cut cases have been reported previously, and the present authors report 5 additional cases.

The onset of the condition, usually in the first 4 months of life, is characterized by irritability and, usually, fever. Then, firm, tender, but diffuse swellings appear deep in the tissues. These are not hot, nor are they red, and they are not associated with adenopathy or fluctuation. At some later time the roentgenogram shows deposits of subperiosteal bone in the areas of swelling, and also in other areas. These vary in size, and they may sometimes be large enough to produce gross deformity. They have been noted in all parts of the skeleton except the spine, pelvis, and the hands and feet. Inconstant associated findings may be fever, leucocytosis, anemia, increased sedimentation rate, and pleurisy. The disease runs its own course with spontaneous cure, regardless of any therapy so far tried. There are many remissions and exacerbations, and various lesions may be at different stages of development at any one time.

The etiology of this condition is unknown, yet there have been exhaustive studies on many of these cases. The health of the parents in all of these cases has been good. There has been no sex preference in this series. It is possible to exclude syphilis, race, or geography as causative factors. Also it is unrelated to rickets, scurvy, tuberculosis, pyogenic infection, allergy, or trauma. No investigator so far has been able to link this disease to virus infection. There is no evidence that the disease is dependent upon any disturbance of mineral metabolism. Alkaline phosphatase has not been markedly elevated. There has been no marked disturbance in vitamin concentration. It seems entirely possible that the disease is not primary in the skeleton at all as most patients have constitutional symptoms and soft tissue inflammation long before any bony change is evident. Perhaps the initial disturbance is in muscle, or even in vessels, which in turn affects the periosteum enough to stimulate it. Such a theory would help to explain the lack of periosteal inflammation or hemorrhage. It would also explain the findings in the few reported muscle biopsies, which have shown evidence of degeneration and changes in vessels. The microscopic studies have revealed that the periosteum is grossly thickened, edematous, vascular and cellular, but not inflamed. The subperiosteal new bone is made up of unorganized trabeculae. The marrow is fibrous and extremely vascular. The osteoclasts are very numerous. This frequency of osteoclasts in the bone-forming stage is surprising.

NEWTON C. MEAD, M.D.

Fibrous Dysplasia of Bone. LYLE W. RUSSELL and FREMONT A. CHANDLER. *J. Bone Surg.*, 1950, 32-A: 323.

The etiology and pathogenesis of solitary and multiple areas of "fibrous dysplasia" have remained obscure, as well as their relationship to Albright's syndrome. This report covers studies on 7 patients with solitary lesions, 3 with multiple lesions, and 1 patient with Albright's syndrome.

Long bones of the lower extremity were most commonly involved, and pain was the common presenting symptom. Five patients had pathological fractures. Four patients, representing all categories, had pigmentation of the skin. Laboratory studies yielded only normal findings except for transient elevation of the alkaline phosphatase for a few days after fracture in 2 instances.

Roentgenograms showed either a unilocular "cystic" formation tending to expand and thin the cortex, or a "ground glass" formation obliterating the medullary space.

Specimens of the osseous tissue of the lesions were obtained from all patients and showed replacement of bone by fibrous connective tissue containing more or less imperfect cancellous bone spicules. In several cases small collections of foam cells were seen.

The diagnosis may sometimes be made from the history (in a child 5 to 15 years of age) of insidious onset of dull pain in an extremity, with or without local tenderness. Trauma or even pathological fracture may first attract attention to the lesion. In many cases, however, symptoms have not been seen until adult life, and roentgenograms followed by biopsy usually lead to the diagnosis.

Resection or curettage of accessible lesions usually relieved pain. Reduction and immobilization of the fractures resulted in good union, although when fractures were recurrent open reduction with bone grafting was done with success. Asymptomatic lesions may disappear spontaneously.

The literature is well summarized, and excellent photomicrographs and roentgenographs illustrate the text, but no light is shed on the pathogenesis of this entity.

FRANCES E. BRENNECKE, M.D.

The Sensitivity and Innervation of the Articular Capsule. J. H. KELLGREN and E. P. SAMUEL. *J. Bone Surg.*, 1950, 32-B: 84.

The sensitivity of fibrous articular ligaments and synovial membrane has been disputed and the contribution made by these structures to joint sensation is uncertain.

Deep sensibility has been separated into two main types, namely, pain and pressure. The authors have studied these sensory modalities in the knee joints of normal human volunteers and in patients undergoing arthrotomy under local anesthesia. Studies were made of the innervation of human and feline knee joints.

The fibrous ligament was found to be a highly sensitive structure containing many spots which give rise to sensations of pain or pressure when stimulated mechanically or chemically. Synovial membrane was found to be a relatively insensitive structure which only occasionally contains pain-sensitive spots.

Histological examination of articular capsule from the knee joints of normal and sympathectomized cats shows that articular ligaments have a rich nerve plexus and a variety of specialized and unspecialized nerve endings, most of which are somatic in origin. Synovial membrane contains a more delicate nerve network and also a variety of nerve endings, the majority of which are autonomic in origin. But a substantial number of somatic nerves enter the synovial membrane, some of which terminate in nerve loops, globular endings, or simple unspecialized endings.

Histological examination of normal human articular capsule shows that its innervation closely resembles that of the cat, but no sympathectomized human material was examined.

The bearing of these findings on the symptomatology of joint disease is discussed briefly.

KENATH H. SPONSEL, M.D.

On Injuries to the Acromioclavicular Joint. ERIK MILLBOURN. *Acta orthop. scand.*, 1950, 19: 349.

Between the years of 1937 and 1946 the author observed 58 cases of acromioclavicular joint injuries at the Lund Surgical Clinic. Fifty-three of the 58 had occurred in men and 5 in women. The average age of the male patients was 37 years and that of the women was 36.

The injuries commonly encountered were divided into two types: (1) mild, or distraction and subluxation, and (2) severe, or luxation with complete dislocation. Forty-five of the 58 cases belonged to the mild type and 13 to the severe type.

The treatment given was conservative in 44 cases, while more radical treatment was required in 14 cases. The conservatively treated cases were managed by sling and adhesive strapping, but without rigid immobilization of the arm in an adducted position.

Another form of conservative treatment was by means of a Frising abduction cushion, which was worn day and night. The Boehler brace was used in 3 of the author's cases. The duration of the disability in the conservatively treated cases was from 6 to 80 days, the average being 23 days. Surgical treatment is not recommended in the mild cases of acromioclavicular injuries.

Of the 13 patients with more severely injured shoulders, i.e., with complete dislocation of the acromioclavicular joint, 7 were subjected to some (varied) surgical therapy. The period of incapacity in the surgically treated cases averaged about 65 days. In 3 of the 7 patients, an extra-articular procedure with wire or fascia lata was performed. An intra-articular procedure was done in the remaining 4 patients.

The results obtained were uniformly good. The functional end results were satisfactory both in the conservatively as well as in the surgically treated cases. Anatomically, the end results were poor in the conservatively treated, and in the intra-articularly treated cases.

A 10 year follow-up study disclosed a high incidence of calcification of the acromioclavicular joints especially in the patients who had been treated with fascia lata suture. An equal number of patients treated conservatively also showed calcification of the joint.

SAMUEL L. GOVERNALE, M.D.

A Case of Synostosis in the Distal Radioulnar Joint. MAC FELLÄNDER. *Acta orthop. scand.*, 1950, 19: 411.

Synostosis of the distal end of the radioulnar joint is rare. Some 200 cases of synostosis of the proximal radioulnar joint, however, have been observed. Most of these have proved to be of congenital origin.

The author reports the only single case of an acquired bridging of the radioulnar joint without involvement of the wrist joint. Arthritis and infections are notorious for their ankylosing effect upon the wrist joint. Synostosis here, however, is tantamount to a contiguous extension of the joint pathology.

The case report is that of a 38 year old female, pianist by profession, who 12 years previously had experienced high fever, tenderness, swelling, and discoloration of left wrist joint. Immobilization of the arm was instituted for a period of 10 weeks. While her general condition improved rapidly, pronation and supination were completely lost.

Because of her occupation, the treatment consisted of resection of the distal end of the ulna and exostectomy. The wrist joint was not opened. Her functional results were excellent.

Ordinarily, unless the patient's occupation makes it mandatory, the author does not advocate any operation for this deformity.

SAMUEL L. GOVERNALE, M.D.

The Endocrine Basis for Slipping of the Upper Femoral Epiphysis. An Experimental Study. W. ROBERT HARRIS. *J. Bone Surg.*, 1950, 32-B: 5.

An endocrine basis for slipping of the upper femoral epiphysis is suggested by the fact that the lesion is nearly always accompanied by abnormalities of growth, probably related to endocrine function. Both growth hormones and sex hormones alter the rate of proliferation of the cartilage cells in the epiphyseal plates. Anterior pituitary growth hormone stimulates the cells directly, with increase in

the thickness of the plates and in the rate of skeletal growth. The sex hormones slow the proliferation of these cells with decrease in the thickness of the plates and in the rate of skeletal growth. It is assumed that an imbalance between these two endocrines is the cause of structural weakness in the epiphyseal plates which makes them more susceptible to shearing stress.

Young albino rats were used throughout the experiment. Three groups were used with equal number of male and female animals in each group. One group was used as controls; a second group was gonadectomized and treated with anterior pituitary growth homones, and the third group was given estradiol benzoate.

An apparatus was designed to test the shearing strength of the upper tibial epiphysis. Stress was such that the projection of the tibial tuberosity was not a factor. One tibia in each rat was tested for shearing stress and the other was prepared for histologic examination.

Shearing tests indicated the following: the control group required 1,150 gm. to displace the epiphyses, the growth hormone-treated animals required 650 gm., and the estrogen-treated animals required 1,870 gm. The results on males and females were statistically similar.

The histologic study indicated that the growth hormone-treated animals had thickening in the layers of proliferating and maturing cartilage cells in the plate. Numerous mitotic figures were found on the epiphyseal side of the plate. The plates from the estrogen-treated animals were much thinner than the control group. The cells in the cartilaginous portion of the plates were irregularly arranged and did not form orderly columns. The trabeculae in the metaphysis were increased both in number and in thickness.

The normal epiphyseal plate of the rat is also described. The layer of hypertrophied cartilage cells next to the epiphyseal side of the provisional zone of calcification was found to be the constant site of separation. The thickness of the layer is altered by each hormone. Estrogen contributes to the narrowing of the hypertrophied cartilage layer, and hence to the strength of the plate.

Previous investigations have shown that the estrogens inhibit the production of growth hormone. In this way estrogens act indirectly upon the epiphyseal plate.

The abnormalities of growth associated with slipping of the upper femoral epiphysis in man suggest that the growth-hormone to sex-hormone ratio has been disturbed in favor of the growth hormone. This could occur in either of two ways: (1) by decreased sex hormone secretion such as occurs in the adiposogenital syndrome, or (2) by increased growth hormone secretion such as occurs in the tall, thin, rapidly growing child.

It is suggested that such a mechanism may operate in cases of slipped upper femoral epiphyses.

KENATH H. SPONSEL, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Improvement of Therapeutic Results in Open Joint Injuries and Suppurations of Joints (Zur Verbesserung der Behandlungsresultate offener Gelenkverletzungen und Gelenkeiterungen). K. LENGGENHAGER. *Helvet. chir. acta*, 1950, 17: 10.

This article is based on observations made for the greatest part before the era of antibiotics and chemotherapy.

The author emphasizes that, in contrast to time-honored beliefs, an open joint injury, if left alone, need not lead to ankylosis. Even without antibiotics and chemotherapy, no infection of the joint will occur if, after careful cleansing of the wound, sufficient drainage is assured by application of vioform gauze drains. Gentle passive and active movements should be started a few days after the injury.

In the cases of infected joint injuries, good functional results can be obtained with generous bilateral opening and drainage. This should be done whenever antibiotics, chemotherapy, or both, have failed to check the suppuration within 3 days. Passive exercises should be started as soon as the patient is afebrile. In infected large articulations traction should be applied to avoid degeneration and necrosis of the cartilage. Unless the pressure on the glenoid cavity is relieved by traction, degeneration may develop rapidly under the toxic influence of pus.

Numerous instructive pictures are added to the article.

WERNER M. SOLMITZ, M.D.

A Preliminary Report on the Use of a Local Flap and Peg Bone Graft for Lengthening a Short Thumb. N. C. HUGHES and F. T. MOORE. *Brit. J. Plast. Surg.*, 1950, 3: 34.

The authors credit Gillies with the first discussion of a hypothetical method of lengthening partially amputated thumbs by local flaps. In the present article the authors report on 2 cases in which the method was used. Although the nerve supply to the skin of the local flap is interrupted, sensation may return to a high degree because the skin possesses normal nerve endings into which nerve fibers may grow. Stability was achieved by cancellous peg bone grafts.

The operation of transforming an index finger into a thumb may be objectionable because it necessitates the patient's learning a new neuromuscular pattern. Other methods, while retaining normal sensation in the new thumb, were thought to be somewhat unsound or complicated and might ignore the normal neuromuscular pattern.

The authors' 2 patients had sustained traumatic amputation of the left thumb at the metacarpophalangeal joint along with injuries to other digits. Both patients were righthanded and were employed on grinding machines. Both worked for small firms, and their posts could not be held open for an indefinite period of time.

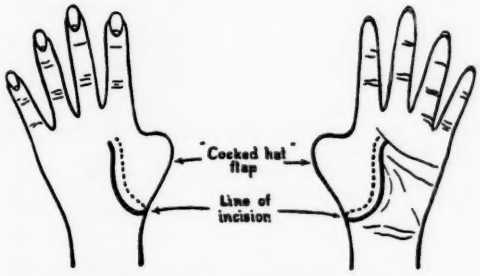


Fig. 1 (Hughes, Moore). Diagrams to show line of incision on the palmar and dorsal surfaces of the hand.

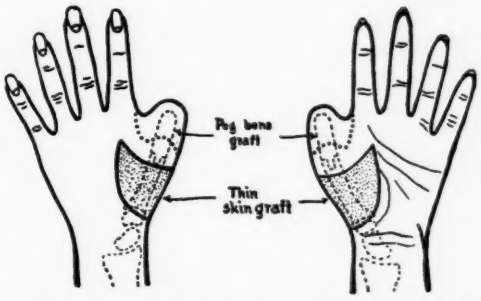


Fig. 2 (Hughes, Moore). Diagram showing peg bone graft in position covered by "cocked hat" flap. Note that the true gain in length of the thumb is camouflaged by the advancement of the thumb web which takes place.

The operation is carried out in a bloodless field secured by a pneumatic type of tourniquet. The cap of normal skin over the amputation stump of the thumb is retained in its entirety in the shape of a "cocked hat." The base or pedicle of the flap is designed with a safe base-to-length ratio and a "delay" is unnecessary. The entire flap is undermined in a plane superficial to the venous plexes, except at the terminal scar where the dissection is completed down to the bone stump so that the entire flap can be "dislocated" from the metacarpal bone.

Next, a block of bone with periosteum attached is cut from the full thickness of the iliac crest and shaped until the bone graft corresponds in thickness to the metacarpal bone. The peg is then carved to a width almost equal to that of the cancellous marrow which has been exposed by shaving off the head of the metacarpal bone with a chisel. The bone graft is cut long enough to project the tip of the new thumb to the level of the metacarpophalangeal joint of the index finger.

The peg bone graft is next firmly impacted into the metacarpal bone of the thumb. The skin flap is transferred over the bone graft. This leaves a raw area crescentic in shape at the base of the original metacarpal bone of the thumb. A part-thickness graft is then sutured in place over the raw area.

While the reported method has not been fully proved and has been employed in only 2 cases, early results justified a preliminary report.

KENNETH E. SHERMAN, M.D.

Osteoarthritis of the Hip Joint, with Special Reference to Treatment by Cup Arthroplasty. WILLIAM H. BICKEL. *Am. J. Surg.*, 1950, 79: 420.

With every step, the hip joint must carry the entire weight of the body. Any limitation in the range of motion or any irregularity of the joint surfaces which causes pain will result in changes in the normal gait ranging from minor to complete disability. The magnitude of the disability from a painful hip, or worse, from two painful hips, cannot be exaggerated. Osteoarthritis of the hip joint, known also as malum coxae senilis, morbus coxae senilis, hypertrophic arthritis, and osteoarthrosis, is a most disabling manifestation of generalized ostecarthritis. It is more common in men than in women. Although it is much more common in later life, it occasionally manifests itself in the younger age groups. It is most frequently unilateral, but bilateral occurrence of osteoarthritis is frequent enough to make treatment a real problem.

There is no specific etiologic factor in osteoarthritis of the hip. Perhaps the most important factor is trauma. There is no doubt that the gradually diminishing blood supply of the hip consequent to age and arteriosclerosis or functional vasoconstriction hastens, perhaps in many cases causes, the degeneration of the articular surfaces. Osteoarthritis certainly develops in hips which have previously been damaged by an infectious process such as that associated with rheumatoid arthritis or with any specific infection.

The fundamental pathologic process in osteoarthritis is the degeneration of the mucinous portion of the hyaline cartilage. This is followed by fibrillation of the cartilage, which is characterized by a splitting of the matrix prior to complete degeneration and wearing away; eventually a sclerotic subchondral bone plate is left and beneath this cystlike cavities may be present. These cysts may form also in the ilium about the acetabulum.

The marginal proliferative bone changes about the acetabulum and head of the femur at the insertion of the periosteum and synovium may be caused by the traumatic hyperemia which occurs in these tissues subsequent to the use of the degenerating joint. Loose flecks or plaques of cartilage and osteocartilaginous loose bodies are not uncommonly found in joints which are undergoing such changes.

Characteristically, there is proliferation of bone with lipping and osteophyte formation. Narrowing of the joint space and marked sclerosis and eburnation of the cortical bone occur. Cystlike areas of degeneration are present about the articular surfaces. The head of the femur enlarges and becomes flattened on the weight-bearing surface, assuming an oval shape. The acetabulum appears large and deep and conforms to the shape of the head of the femur.

Just when the onset of osteoarthritis in a hip occurs is difficult to state. Many such lesions observed roentgenologically in their inception are asymptomatic, but on physical examination one will find some limitation of rotation in the hip. Slowly, progressively, and insidiously, the process goes on until pain and marked limitation of motion are present. Deformity in the form of adduction and flexion of the hip may take place.

Conservative treatment of osteoarthritis of the hip is designed purely to decrease the wear and tear on the hip joint and to relieve the pain and the muscle spasm. It consists of weight reduction in heavy individuals, avoidance of long hours of standing and walking, and the use of a cane or a crutch. Heat, massage, and aspirin are about the only agents available for the relief of pain and muscle spasm. Occasionally, changing the relationship of the weight-bearing surfaces of the hip joint by a lift on one heel will help temporarily.

The most certain way to relieve pain and deformity in a hip affected with osteoarthritis is by arthrodesis, with the joint fixed in good position. In a person who subjects his hips to hard use arthrodesis should be done. Several things, however, mitigate against this procedure: (1) patients with a surgically ankylosed hip are somewhat clumsy, and some inconveniences attend a stiff hip; (2) in many patients with osteoarthritis both hips are involved, and it is difficult to predict when unilateral disease will become bilateral; and (3) a surgically ankylosed hip will not be accepted by some individuals; consequently various operations have been designed to relieve symptoms and deformity and yet to permit maintenance of motion.

Operations designed to increase the circulation of the head and neck of the femur are (1) the drilling of multiple holes from the trochanteric region into the neck and head of the femur, and (2) a guttering operation on the neck of the femur into which a pedicle of muscle is inserted. Temporary and occasionally permanent relief of symptoms is reported, but the results have not been very satisfactory.

Partial denervation of the hip joints by sectioning the obturator nerve either by an intrapelvic or an extrapelvic approach has been done for some time and recently has come in for much consideration. On occasion, the posterior sensory nerves to the hip joint arising from the sciatic nerve have also been sectioned. The results have not been consistent or predictable in the relatively small series of cases that have been reported. In a few cases the author and his associates have attempted, by obturator neurectomy, to relieve pain following cup arthroplasty but the results have not been good.

Osteotomy of the upper end of the femur to change the relationship of the weight-bearing surfaces of the hip joint has been done and is being done for pain in the hip. While it must be admitted that in some cases the pain is relieved, it is difficult to believe that the relief will be permanent in such a mechanically unsound and incongruous joint.

Cheilotomy and acetabuloplasty have not proved satisfactory in the long run.

Arthroplasty of the hip joint has been done for years, with or without interposing membranes, but the results have not been sufficiently encouraging for this procedure to find many advocates until the advent of the vitallium mold as developed by Smith-Petersen.

From the figures presented in the original article, cup arthroplasty of the hip still leaves something to be desired. With better selection of patients, with better operative technique, and with time and use of the operative hip there appears to be some reason to believe that results will improve. The figures reported were obtained in spite of the fact that the condition of the 5 patients became worse because of lucite cups, two of which were proved, on exploration, to be fractured.

The author reports that the condition of 5 other patients had improved in the past 3 years.

It is believed that cup arthroplasty has a very definite place in the treatment of osteoarthritis of the hip joint.

Plastic Replacement of Torn Cruciate Ligaments by Pedicled Tendon Transposition (Ueber den plastischen Ersatz der Kreuzbaender durch gestielte Sehnenverpflanzung). KURT LINDEMANN. *Zschr. Orthop.*, 1950, 79: 316.

The diagnosis of an old tear of the cruciate ligaments is made when there is atrophy of the leg muscles, a feeling of weakness, and insecurity of the knee joint. The inability to bear weight on the knee joint in a semiflexed position also is a valuable diagnostic sign. The primary repair of the torn cruciate ligaments is occasionally found to be successful.

In 1932 Wittek sutured the torn anterior cruciate ligament to the posterior ligament with good results. Bircher in 1933 replaced the torn cruciate ligaments with beef fascia. Lange also transplanted fascia taken from the lateral iliotibial band with its distal portion left attached. This treatment is reported to be very successful. Felsenreich uses the gracilis muscle, and occasionally the semitendinosus muscle to replace the torn cruciate ligaments by leaving the insertion of the tendon intact. In all instances the feeling of weakness disappeared and the push and pull sign could not be elicited postoperatively. A parapatellar incision was made and carried down into the knee joint. A second incision was made along the course of the gracilis muscle. The tendon was severed at its point of insertion and dissected free to the level of Hunter's canal. The end of the tendon was pulled anteriorly through a hole made in the posterior aspect of the capsule. The tendon was then pulled through a hole in the anterior position of the tibial condyle and sutured somewhat medial to the tibial tubercle. In the replacement of the torn posterior cruciate ligament the gracilis tendon was fixed to the posterior aspect of the tibial condyle. A plaster cast was applied for 3 weeks. The

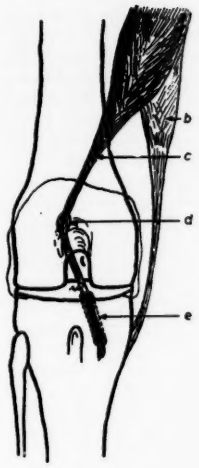


Fig. 1.

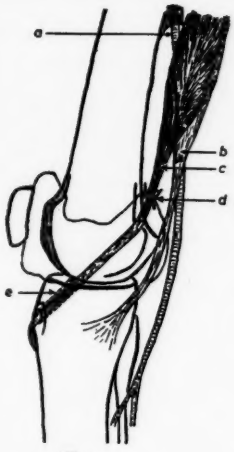


Fig. 2.

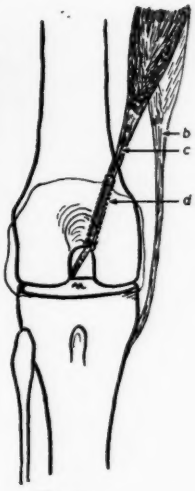


Fig. 3.

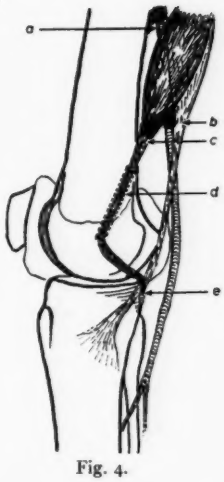


Fig. 4.

Fig. 1 (Lindemann). *b*, The original course of the gracilis tendon. *c*, The course of the gracilis tendon transplanted to the posterior aspect of the thigh. *d*, The entrance of the tendon into the posterior aspect of the capsule. *e*, Canal drilled through tibial condyle with tendon *in situ*. A diagram illustrating the replacing of the anterior cruciate ligament by the gracilis tendon.

Fig. 2. Diagram of the lateral view. *a*, The diagonal course of the transplanted tendon through the knee joint between *d* and *e*.

Fig. 3 (Lindemann). Diagram: Replacement of the posterior cruciate ligament. The oblique canal within the medial condyle of the femur. The oblique course of the tendon within the knee joint corresponds to the course of the posterior cruciate ligament.

Fig. 4. As seen in Figure 3, the muscles and the tendon were placed on the medial aspect of the medial condyle; *e* corresponds to the insertion of the tendon at the posterior origin of the decussating ligament on the posterior aspect of the tibial condyle.

cast was then bilvalved and active and passive exercises were started with no weight bearing.

GEORGE I. REISS, M.D.

FRACTURES AND DISLOCATIONS

Medial Epicondyle Injuries. FREDERICK M. SMITH. *J. Am. M. Ass.*, 1950, 142: 396.

It is pointed out that injuries to the medial epicondyle of the humerus are common, though usually not as serious as they appear to be in the general opinion of practitioners. It is important to note whether or not the epicondyle has been displaced into the elbow joint, as conservative treatment will be successful in cases in which this has not occurred. Where there has been displacement of the fragment into the joint, open operation through a medial incision must be done to remove this fragment, and it may then be reattached to its normal site on the humerus by sutures or nails, or it may be excised and the muscles attached to the former site of the epicondyle.

The diagnosis of elbow injuries in children is not complete until all of the ossification centers have been accounted for, and are found to be in their proper positions.

Conservative treatment is indicated in all cases of epicondylar displacement except those which become intra-articular, or in which ulnar nerve damage has taken place. The period of immobilization should be as short as the symptoms will permit, and early active exercises within the limits of pain should be started. The status of the ulnar nerve should be observed and frequently checked during treatment, and, should it be contused or otherwise damaged, it is wise to transpose it to the anterior surface of the reattached muscles, to avoid the possibility of its becoming fixed in scar, and also to provide relaxation for it. The author makes use of the injection of isotonic sodium chloride into the nerve sheath as a prophylactic against fibrosis within this sheath. The prognosis is excellent if the condition is treated early and is not overtreated.

NEWTON C. MEAD, M.D.

Concerning the Opportunity of Suture in Open Fractures and Grave Traumatisms of the Extremities (Sobre la oportunidad de la sutura en las fracturas expuestas y en los traumatismos graves de los miembros). CARLOS E. OTTOLENGHI. *Rev. As. méd. argent.*, 1950, 64: 1.

The treatment of open fractures is one of extreme urgency and the surgeon must make it a race against infection, since the area of these fractures must be regarded as contaminated within 6 to 8 hours of the

accident and as infected after this interval. The antibiotics, especially penicillin, delay bacterial reproduction and allow more time in which to act, but the rules given still stand and have not been disproved. All authors agree that the first surgical procedure will be decisive for the patient. Treatment must be complete and in accordance with the following five principles laid down by Trueta: immediate surgical intervention, cleaning of the wound, resection of the contused tissues, drainage, and immobilization.

When the soft tissues and the bone have been attended to, the surgeon must decide whether to close the wound or not. Primary suture is permissible only under the following conditions: (1) when the case is recent, not more than 8 hours having elapsed since the accident; (2) when there is no marked contusion of the soft tissues; (3) when total excision of the dead tissue and foreign bodies has been done; (4) when there is a good local and peripheral circulation; (5) the skin must have a normal appearance; (6) when suture can be made without tension and without dead spaces; (7) when operation can be done in organized surroundings by an experienced surgeon and under conditions in which the patient can be carefully watched postoperatively; and (8) when the patient will remain in the hospital where the emergency operation took place.

Primary suture is the ideal treatment of open fractures, but it is dangerous and the patient will run less risk if the area is left open. The author believes that in many cases some of the rules are forgotten which accounts for the failures encountered. A striking fact observed by him is that in practically 100 per cent of the cases which reach him after having been treated the wound has been closed. This is certainly not justifiable.

Experience in the last war has demonstrated the value of delayed suture of wounds. Unless the mentioned conditions are fulfilled, the wound should be left open. This attitude provides a safety valve and protects the patient against infection with resulting gangrene, osteomyelitis, or phlegmon. Leaving the area open offers practically no inconvenience provided the excision has been carefully done; in a second stage of the operation between the fifth and fifteenth days after the first operation, secondary suture is performed which affords perfect healing of the wound, or a plastic operation is done in cases in which loss of skin requires it. Various cases are cited in support of these remarks.

RICHARD KEMEL, M.D.

Extended Indication for Fracture Treatment with Parallel Wire Transverse Counterpull (Erweiterte Indikation fuer die Knochenbruchbehandlung mit parallelen Drahtquergegenzuegen). H. B. KEMKES. *Chirurg*, 1950, 21: 40.

Two parallel stainless steel wires, 1 to 2 cm. apart, are drilled through the fragments of the fracture in such a manner as to meet the fracture plane as perpendicularly as possible. With special pliers a bayonet-shaped sharp bend is made on opposite sides of the two wires close to the skin and the unchanged side of each wire is fastened to a Kirschner tension stirrup. The bayonet-shaped bends cut through the soft tissues and end at the bone surface, but their continued pull presses the fragments together. When the tension possibilities of the stirrup are exhausted before the bayonet-shaped bends reach the bone, the stirrup is loosened and replaced under tension. Removal of the wires is easily accomplished in the opposite direction provided the ends of the wires on the bent side protrude sufficiently from the skin surface.

The use of the method depends on the topographic possibilities. The most appropriate fractures for this treatment are those of the tibial shaft and head, in which excellent results are obtained. Kemkes sees an extended indication of the method in the cases in which a fracture must be surgically reduced for any reason whatever. For instance, when an isolated tibial shaft fracture cannot be reduced or does not form a callus, there is usually an impediment in the form of a bone block (intact fibula) or of interposed soft tissues which requires surgical correction. Under the circumstances the parallel wires can be inserted under visual control. It will often be unnecessary to perform osteotomy of the blocking fibula. In cases of pseudarthrosis after the ends of the fragments have been freshened, it will also be advantageous to obtain exact adaptation of the fragments under visual control. The fracture fixed by this method is placed on a plaster or Braun splint to wait for callus formation.

The advantages of the method are its technical simplicity, its reliability, and the absence of danger to the patient. The method avoids the error inherent in the various traction apparatuses which may pull the fragments too far apart. The exact fixation of the fracture shortens its healing period, and the presence of a minimum of foreign substance does not interfere with callus formation. The disadvantage of the method lies in its limited applicability since its use is practically reduced to the lower extremity. The method is particularly well adapted to render good services in the torsion fractures of the lower extremities of skiers. Even in transverse fractures of the tibia the author has succeeded in using the method when the parallel wires reached the fracture plane at an angle of about 45 degrees. He has obtained excellent results in transverse fracture of the olecranon by inserting the wires along the longitudinal axis of the ulna. The so-called drill-hole osteomyelitis can be avoided by clean work, sufficient tension on the wires to avoid displacement of the fragments, and timely removal of the wires.

RICHARD KEMEL, M.D.

The Reduction of Fractures of the Forearm by Direct Leverage (Le réduction des fractures de l'avant-bras par le levier démonte-pneu). FERNANDO DE MORAES. *Acta orthop. belg.*, 1950, 16: 5.

Direct leverage for reduction of fractures of the forearm was first described by Thompson (*J.*

Bone Surg., 1936, 19: 397). He did not employ preliminary traction but used a dental instrument to implement the leverage. In 1940 Rocher of Bordeaux described this same technique and used the term "démonte-pneu" to designate the method.

In the region where the author is located (Brazil) the frequency of these injuries (which are 2 or more days old when reaching the hands of the orthopedic surgeon) has resulted in the introduction of gentle, continuous traction (method of Weinbert or of Sokolowsky) before the operation is attempted.

When the fragments are more or less on the same level a puncture-incision is made with a tenotome over the dorsal surface of the broken radius or ulna, the site depending upon the predominant deviation of the fragments. The incision should be placed somewhat lower than the level of the fracture. The tenotome is inserted obliquely, so that after the operation is finished the tissue planes will more or less come to overlap and thus obliterate the line of incision. After the tenotome is withdrawn, a stylet, or a thin Steinmann nail (4 mm.) with a sharp point is inserted between the fracture surfaces and used as a lever, under control of the fluoroscope, to reduce the fracture fragments. In some instances the stylet, or nail, is carried through an arc of 180 degrees before the reduction is obtained.

When reduction is obtained and checked by means of the fluoroscope, the part is immobilized in an unpadded plaster cast, the stylet, or nail, having been withdrawn. The author sees no reason for leaving the stylet in place and embedding it in the cast as has been done by both Thompson and Rocher.

Five children, ranging in age from 4 to 15 years, with neglected fractures (2 to 7 days) have been treated in the author's service with this method. Roentgenographic reproductions in the original text show the excellence of the results obtained.

Advantages of the method are absence of scar, small liability of infection, reliable bony consolidation, minimum demands for anesthesia (the operation can be done under local anesthesia), treatment may be ambulatory if the skill of the surgeon is adequate, and, most important, the financial outlay is minimal.

Despite the progress in the methods of traction in these fractures, recourse must be had to open operation; and this nonmutilating and reliable method can be recommended. JOHN W. BRENNAN, M.D.

A Critical Consideration of Primary Subtrochanteric Osteotomy and Internal Fixation for Recent Intracapsular Fractures of the Femoral Neck. THOMAS KING. *Austral. N. Zealand J. Surg.*, 1950, 19: 177.

The operation of primary subtrochanteric osteotomy with internal fixation of the reduced intracapsular femoral fracture has been proposed by several surgeons in recent years and has been used by the author for a period of 3 years in the treatment of all fractures of this type unless the patient was moribund. The first 50 consecutive patients so treated are reported upon. The advantages have been that (1) the fracture line becomes almost horizontal when the 125 degree angle plate is attached to the nail in the femoral head, and after osteotomy the fragments are adducted; (2) weight-bearing is transferred to the lateral pelvic wall below the acetabulum and underneath the fracture line; (3) the occurrence of avascular necrosis has been only 4 per cent as compared to 28 per cent after nailing alone.

Certain disadvantages of the procedure have been: (1) nonunion at the osteotomy site in 5 per cent of 140 subtrochanteric osteotomies for various conditions, and in cases in which only external splinting was used (not at all in the present series), internal fixation was used after impacting the femoral shaft into the base of the trochanter; (2) no improvement in the percentage of bone union at the fracture site over that obtained by nailing, with or without grafting, i.e., 70 per cent. Contrary to the experience of some writers, when nonunion of the fracture occurred the functional result in the osteotomized patients was poor or bad, pain and weakness being the chief difficulties. No greater shock was incurred during the additional surgery, nor were there any instances of infection. All were treated with penicillin and sulfonamides.

Special features of the technique of operation are adequately explained and demonstrated by numerous diagrams. The peculiar advantage of primary osteotomy in the author's hands has been the low incidence of aseptic necrosis of the femoral head.

FRANCES E. BRENNECKE, M.D.

Anterior Isolated Luxation of the Head of the Fibula (Lussazione anteriore isolata della testa del perone). PIER LUIGI BISOTTI. *Riforma med.*, 1950, 64: 80.

In a sports contest the 25 year old patient caught the ball with the left foot and kicked it across to a companion, then made the movements of return to the original position. In doing this, however, his right foot was impeded in the twisting movement by the foot of a fellow player. Thus the right knee and thigh underwent a movement of torsion internally, the right foot being unable to follow. It was with this motion that the acute pain was felt and the patient was unable to rise to his feet again.

Upon arrival at the hospital the head of the fibula could be felt in front of and above the tuberosity of the tibia. It was painful to palpation. At the normal position of the fibula with reference to the superior tibiofibular joint there was a flat depressed surface. Passing across this obliquely from above downward and forward was a tense, thick cord, the tendon of the biceps femoris muscle. The axis of the fibula and that of the tibia formed an acute angle which was open upward. The knee joint itself was not painful; however, it could be flexed actively but little and could not be fully extended.

Roentgenologic examination disclosed the head of the fibula displaced laterally and forward, forming an angle of about 10 degrees with the tibia.

Treatment under novocain local anesthesia consisted in continuous pressure with both thumbs of

the operator in a direction from the front backward, an assistant meanwhile exerting traction and attempting to evert the leg with respect to the thigh which was held firmly by a second assistant. After a minute or so of such manipulative effort the fibular head suddenly slid posteriorly with a detectable snap. Roentgenology showed that the fibular head was still not entirely replaced. That same day the patient who was getting about on crutches slipped and involuntarily put down the involved foot for support. Immediately there was a violent pain in the affected knee. The clinical and roentgenological examination now disclosed the fact that the head of the fibula had returned to its normal position. A plaster splint was applied for 20 days.

After dismissal with removal of the splint the joint had become perfectly mobile again and there was very little sensitiveness over the affected fibular head. The patient was advised to wear an elastic bandage.

This case is fully reported because of the slightly different *modus* of the injury, because the patient was able to relate the details of the happening with perfect clarity, and because very little has been said about this dislocation (especially in the Italian language), in the current text books on dislocations and fractures. JOHN W. BRENNAN, M.D.

ORTHOPEDICS IN GENERAL

Function of the Sulfuric Esters of High Molecular Weight in Heterotopic Ossification (Funzione degli esteri solforici ad alto peso molecolare nell'ossificazione eterotopica). P. LI VOTI. *Ann. ital. chir.*, 1949, 26: 494.

In the present experimental study, the authors used 8 dogs of average size. These animals were kept on a mixed diet. Through a median suprapubic laparotomy, he exteriorized the bladder and, under maximal aseptic precautions, excised a lozenge of tissue which he washed in sterile physiologic salt solution; the bladder and abdominal wall were closed in layers. The mucosa of the specimen was detached from the muscular layer and fragments of mucosa, about 1 by 1 cm. in size, were grafted into the neck muscles of the same animal. All wounds healed by first intention and the animals were killed in groups of two, after 10, 20, 25, and 30 days, these periods being selected to avoid the necessity of prolonged decalcification which would have an injurious influence on the subsequent histologic treatment. Specimens taken from the implantation zones were fixed and stained according to Holmgren and Wilander's technique which allows preservation in the histologic sections of the sulfuric esters responsible for the metachromatic staining with toluidine blue. The findings were as follows:

1. In the first 10 days, the implanted epithelium undergoes degenerative changes which determine in it the appearance of metachromasia, probably attributable to the presence of mucoid in sulfuric acid formed as a result of the mucosal degeneration.

2. Between the tenth and twentieth days, mast cells rich in intracellular granula metachromatic substance (polymucoidin sulfuric acid) appear in great numbers in the peripheral zone of the reaction tissue formed around the implant; simultaneously there is metachromasia in the collagen fibers of the zone destined to be transformed into osteoid tissue.

3. With the appearance of bone, there is a tendency to diminution of the mast cells while the diffuse metachromasia of the osteoid tissue disappears gradually and persists only in the bone of more recent formation.

4. This confirms the hypothesis that bone formation, even when it does not follow a cartilaginous phase, is preceded by imbibition of the tissue with sulfuric esters of high molecular weight, which, in the case of cartilage, consist of chondroitin sulfuric acid, and in the other case, of mucoidin sulfuric acid. It is probable that these substances are delivered to the fibrillary tissue and then to the ossifiable amorphous substance deriving from it, through the mast cells, in analogy with the observations of Sylvén in neoplasms.

5. Thus it seems probable that the sulfuric esters of high molecular weight constitute one (if not the principal one) of the factors determining the ossifying power of the tissues, and that their presence is the essential element to make it possible for the alkaline phosphatases to exercise their function and for deposition of calcium salts in the tissue to occur. RICHARD KEMEL, M.D.

Arteriography in Bone Tumors. REYNALDO DOS SANTOS. *J. Bone Surg.*, 1950, 32-B: 17.

The author has studied 100 cases of tumors of the extremities and many cases of chronic osteomyelitis by simple arteriography with the aid of serial roentgenograms.

To understand the arteriography of bone tumors, comparisons were made with normal arteriograms, those of soft tissue tumors, and those of inflammatory lesions.

Sarcomas arising from soft tissues of the thigh show a rich vascular network of hairy appearance arising from the deep femoral artery, together with a tangled mass of new vessels, nearly all of the same diameter. In contrast, inflammatory lesions are associated with simple hyperemia in which the arterial pattern retains an orderly and regular arrangement with successive branches of decreasing diameter. In other examples, the vascular network of a tumor, usually a sarcoma, shows multiple dilatations with the formation of "blood pools" which again are a consequence of new tissue formation.

In new growths the blood passes almost directly into the veins without interposition of capillaries. An increased speed of arteriovenous flow is one of the most constant features of the circulation of tumors, particularly sarcomas of the bone and soft tissue. The first veins to be filled may be seen to arise directly from the tumor itself. The abnormal vascular pattern defines clearly the limits of the tumor,

the extent of which is seldom disclosed by routine radiographs.

Blood pools are often seen in osteoclastomas. Filling of the venous tree is less rapid than in sarcomas, this being a sign of relative benignity. Radiographic examination one or more months after arteriography showed that the tumor was still impregnated with thorotrast.

Arteriograms in chronic osteomyelitis show relative ischemia at the level of the bone lesion, which is in distinct contrast to the newly formed circulation of tumors.

Whereas, in malignant tumors new formations of vessels and early filling of the veins are prominent features, these features are not seen in benign tumors. The greater the activity of the malignant tumors, the more pronounced is the new formation of vessels, and the more rapid is the filling of the veins.

Arteriography may be used to assess the response of the tumor to irradiation. After successful irradiation, the arteriogram assumes a more normal appearance.

Twenty-six illustrative roentgenograms are reproduced. KENATH H. SPONSEL, M.D.

A Clinical Analysis of 205 Cases of Malignant Bone Tumor. SAMUEL BRADLEY PREVO. *J. Bone Surg.*, 1950, 32-A: 298.

Few large series of bone tumors correlating pathologic material with clinical material have been reported. The present analysis includes only cases of bone tumor diagnosed by biopsy and adequately followed. About 0.8 per cent of all orthopedic patients seen at the Campbell Clinic were suffering from some type of bone tumor, and of 702 tumors, 415 were considered malignant. These have been divided as follows: 152 osteogenic sarcomas, 163 metastatic tumors, 65 Ewing's tumors, 24 fibrosarcomas, and 11 multiple myelomas. The highest incidence occurred in the second decade and the next highest in the third decade; relatively few cases occurred in any other age group.

There were 55 cases of Ewing's tumor, 42 cases of metastatic tumors, 41 cases of osteogenic sarcoma, 30 cases each of chondromyxosarcomas and fibrosarcomas, and 7 cases of multiple myelomas. Five year cures are recorded in 1 case of Ewing's tumor, 2 cases of osteogenic sarcoma, 4 cases of chondromyxosarcoma, and 1 case of fibrosarcoma.

An analysis has been made as to the duration of symptoms before the onset of treatment and the duration of life from the onset of symptoms in patients with various types of tumor. In respect to Ewing's tumor, the duration of life of patients in whom early amputation was done was much longer (40.5 months) from the onset of symptoms than that of patients treated by roentgen therapy only (24.7 months). There were no recoveries encountered among the patients presenting either metastatic tumors or multiple myelomas.

FRANCES E. BRENNECKE, M.D.

Physiologic and Morphologic Modifications of Striated Muscles after Intra-Arterial Injections of Organic Iodine Product into the Brachial Artery of Dogs. Experimental Volkmann's Disease (Modifications physiologiques et morphologiques du muscle strié après injections intra-artérielles d'un produit iodo-organique dans l'artère humérale du chien. La maladie de Volkmann expérimentale.) R. FONTAINE, CH. KAYSER, M. KLEIN, CH. MARX, and A. DANY. *Rev. chir.*, Par., 1950, 69: 15.

Volkmann's syndrome, observed chiefly after certain types of supracondylar fractures in children, is characterized by contractures of the muscles, and sclerosis.

The authors observed a typical Volkmann's contracture, which lasted 10 minutes, in a patient who for the purpose of cholecystography was inadvertently given an injection of an organic iodine product into the brachial artery instead of an intravenous injection.

This observation suggested the following experiments. An organic iodine preparation with spasmogenic properties, called tenebryl, was injected into the brachial artery of dogs. The injection was followed by violent pains, disappearance of the peripheral pulse, lowering of the temperature of the plantar surface, and a strong contraction of the epitrochlear muscles. The contracture, causing a flexion of the corresponding paw, was recorded with a cathode oscillograph. It appeared 4 seconds after the injection, and lasted from 15 to 30 minutes, in accordance with the dose of the compound, and could be reproduced by a second injection. After section of the nerves, the contracture was less intensive, lasted a shorter period of time, and could not be reproduced by a second injection.

The experimentally produced contractures were the sequel of a reflex and a peripheral mechanism. The afferent paths of the reflex pass the posterior roots. The sympathetic chain does not participate in this reflex: stellectomy combined with resection of the second and third thoracic ganglia does not modify the contracture. The latter fact is not due to excitation of the endothelium of the large arteries or to irritation of the nerve trunks. Tenebryl has a peripheral effect; it acts directly on the muscle tissue and its sensory receptors.

JOSEPH K. NARAT, M.D.

Radiation Scoliosis. An Experimental Study. ALVIN M. ARKIN and NORMAN SIMON. *J. Bone Surg.*, 1950, 32-A: 396.

Experimental scoliosis has been produced in two ways—indirectly by asymmetrical pressure on the vertebral bodies, and directly by destruction of epiphyses.

The authors have effected spinal epiphyseal growth disturbances by implantation of radon seeds and by the use of roentgen-ray beams. The present study was carried out on growing rabbits.

Irradiation resulted in wedging of the vertebrae. The intervertebral discs were wider at the concavity

of the curves, illustrating nature's attempt at functional compensation of the spine. Histologic study indicated that the deformity was caused by asymmetrical arrestment of epiphyseal growth. None of the animals showed gross or microscopic evidence of necrosis, marrow fibrosis, or inflammatory infiltration.

By this method, direct unilateral suppression of epiphseal growth can be controlled to produce wedging in a predictable area, an effect which may be applicable to treatment of clinical scoliosis.

KENATH H. SPONSEL, M.D.

Neonatal Sciatic Palsy. W. H. FAHRNI. *J. Bone Surg.*, 1950, 32-B: 42.

The author observed 11 infants with neonatal palsy. These cases occurred between April, 1945 and January, 1948 at the Walton Hospital, Liverpool, England.

Because of the paucity of similar cases in the literature, he was led to study and report this problem.

Careful analysis of the cases from every angle disclosed that the common feature of all the newly born infants was a state of asphyxia livida or pallida. The condition responded slowly to clearing of the air passages and the injection of a restorative drug into the umbilical cord.

On examination of each infant, one lower extremity was seen to be limp and the buttock usually showed a bruise. The paralysis was always of the peripheral type, none showing spastic paralysis or a progressive nerve lesion. The day of delivery the infant's buttock and thigh often showed edema in the area surrounding the bruise. There were no fractures. Sloughs occurred in the buttocks in 5 patients. One patient with a slough died secondary to toxemia and dehydration.

Of the 10 survivors, only 3 recovered normal limb function; 7 had residual paralyses and underdeveloped extremities.

The following commentary by Bryan McFarland is quoted:

"The editor's attention was arrested by such a large series of a condition about which he had no knowledge. Comparative statistics from other maternity hospitals revealed no similar cases.

"Austin O'Malley investigated the conditions at the Walton Hospital. He noticed that the routine treatment of neonatal asphyxia included the injection of a certain proprietary drug into the umbilical cord. In other maternity hospitals a different proprietary drug was so injected.

"It may seem a far cry from the umbilical cord to the sciatic nerve, but actually the connection is not so remote. The hypogastric artery coming into the cord runs into the internal iliac artery; and in the fetus this is a larger vessel than the external iliac artery. Below the entry of the hypogastric artery, the next branch of any size to leave the internal iliac is the inferior gluteal artery. If the fluid left the internal iliac artery by the first branch, it would be concentrated in the tissues immediately supplied by the inferior gluteal artery which includes part of the sciatic nerve, the muscles, and the lower half of the gluteal region—in fact, the very zone in which Fahrni found his lesion. This would only occur when the needle entered the umbilical artery and sufficient fluid was concentrated in this area.

"Two years have elapsed since the use of this drug was suspended and no other case of neonatal sciatic palsy has been noted at this hospital."

The commentator is satisfied that injection of this drug was etiologic in the development of the palsies and sloughs. KENATH H. SPONSEL, M.D.

SURGERY OF THE BLOOD AND LYMPH SYSTEMS

BLOOD VESSELS

Complications of Arteriography. Case of Acute Gangrene with Fatal Outcome (Sur les accidents de l'artériographie. Un cas de gangrène aigue a évolution mortelle). R. JOYEUX, A. BISCAYE, and G. CARLI. *Sem. hôp. Paris*, 1950, 26: 948.

Arteriography is indispensable for the establishment of indications for surgical intervention in arteritis. Unfortunately the method is not devoid of danger.

In a woman, aged 54 years, with circulatory disturbances of the left lower extremity, the essential findings were as follows: hypertension, presystolic gallop, normal electrocardiogram, renal involvement, arteritis of the left lower extremity, and questionable serologic reactions.

Eight cubic centimeters of an organic iodine preparation, called tenebryl, followed by 20 c.c. of a 1 per cent novocain solution, were injected into the femoral artery. An obstruction of the left femoral artery in Hunter's canal was demonstrated. Four hours after the injection the blood pressure suddenly fell, and a violent pain occurred in the involved extremity. The pain was not relieved by sedatives, 2 injections of 20 c.c. of a 1 per cent novocain solution into the femoral artery, or sympathetic lumbar block. Cyanosis, ecchymotic patches, phlyctenulae of the involved extremity, and an ulceration in the gluteal region developed in spite of the administration of penicillin and sulfonamides. Amputation was performed and a blood transfusion was given. Hemoglobinuria and jaundice developed and the patient expired 17 days after the operation.

The authors are of the opinion that local intravascular hypertension, provoked by the injection, in the presence of a thrombosis was responsible for the untoward effect of arteriography.

JOSEPH K. NARAT, M.D.

Spontaneous Cure of Aneurysms and Arteriovenous Fistulas, with Some Notes on Intrasaccular Thrombosis. HARRIS B. SHUMACKER, JR., and EDWARD H. WAYSON. *Am. J. Surg.*, 1950. 79: 532.

This study is based upon an analysis of 122 arterial aneurysms and 245 arteriovenous fistulas, many of which were asociated with saccular aneurysms. Nearly all of them occurred in soldiers and, save for 7 fistulas which were congenital in origin and 8 aneurysms which developed as the result of disease or infection or were of unknown etiology, they were traumatic in nature. All of the patients were operated upon except those in whom an apparently satisfactory cure occurred spontaneously. Sixty-three patients had been operated upon prior to this study. Patients with aortic aneurysms and innominate aneurysms treated by wiring are not included.

The authors find that spontaneous cures of peripheral aneurysms and arteriovenous fistulas occasionally occur. This obliteration of the lesion appears generally to result from thrombosis. In the group of cases studied no specific factors responsible for the occurrence of such cures were evident. In most cases such cures are clinically satisfactory, although sometimes subsequent operative treatment is required because of the persistence of a clotted aneurysmal sac or of a pulsating aneurysm associated with a thrombosed arteriovenous fistula. Satisfactory spontaneous cures occurred in the authors' series of arteriovenous fistulas so infrequently (2 per cent) as to make consideration of this possibility of little or no importance in reaching a decision as to the necessity and the proper time for surgical treatment of the lesion. Such satisfactory cures occurred slightly more often in the cases of arterial aneurysm (6.6 per cent), but again so infrequently that their possible occurrence can be given only slight weight in evaluating the problem of treatment. BENJAMIN GOLDMAN, M.D.

Peripheral Arterial Embolism. A Study of 330 Unselected Cases of Embolism of the Extremities. HENRY HAIMOVICI. *Angiology*, 1950, 1: 20.

In this study of 330 unselected cases of peripheral arterial embolism the heart was the source of the embolism in 96 per cent of the cases. Auricular fibrillation accompanying rheumatic heart disease was the most common cardiac condition present, and mural thrombi associated with myocardial infarction was second.

When sudden arterial occlusion occurred in the absence of evidence of heart disease the condition was usually diagnosed as acute arterial thrombosis.

Eighty-four per cent of the emboli occurred in the lower extremities and 16 per cent in the upper. Multiple emboli are not infrequent. The 228 patients in this series had a total of 443 emboli, peripheral and visceral.

The ages of the patients varied from 12 to 85 years. There was a slight preponderance of females over males.

There are four important events which accompany the blocking of an artery by an embolus. First is the mechanical blocking of the artery; second, vasospasm and accompanying ischemia; third, secondary thrombosis which may spread proximally or distally and, fourth, structural changes which take place in the wall of the occluded artery.

The onset of clinical manifestations varied. It was sudden in 81.2 per cent of the patients, of whom 59.5 per cent had sudden pain and 21.7 per cent had sudden numbness and coldness without initial pain. A gradual progressive onset was noted in 11.7 per cent of the patients, and in 5.7 per cent the occlusion was silent.

The author presents a classification of the clinical forms of the disease. The classification is based on the degree of restoration of the circulation: (1) embolism with marked ischemia and early death occurred in 11.3 per cent of cases; (2) embolism followed by gangrene occurred in 28 per cent of cases; (3) embolism followed by incomplete recovery, resulting in chronic postembolic ischemia occurred in 16.5 per cent; (4) embolism was followed by complete recovery in 29.5 per cent; (5) silent embolism occurred in 5.7 per cent.

Concurrent venous thrombosis with arterial embolism was present in 7 per cent of the cases.

The prognosis as to the survival of the extremity depends essentially on the site of occlusion and the promptness of the treatment. The prognosis as to survival of the patient depends upon his heart condition and the possibility of further embolism to vital viscera. Hospital mortality in this series was about 50 per cent.

The results in 300 nonsurgically and 30 surgically treated patients were reviewed. This study reemphasizes the need for immediate institution of therapy, hospitalization of the patient, importance of teamwork between the physician and vascular surgeon, and the avoidance of harmful procedures.

Among the medical measures, vasodilatation induced by drugs or by sympathetic nerve block and anticoagulant therapy are the most valuable.

If these measures fail to restore the collateral circulation within 2 to 4 hours, embolectomy should be performed without any further delay, whenever possible. Arteriectomy and sympathectomy may be useful in a number of cases; their indications were reviewed. FREDERICK W. PRESTON, M.D.

Splitting of the Adductor Canal; a Method of Improving Locally the Collateral Circulation in Thrombangiitis Obliterans. HANS NOVOTNY. *Acta chir. scand.*, 1950, 99: 332.

There is a normal gliding mechanism between the adductor canal and the femoral artery which is disturbed in patients with thromboangiitis obliterans. Splitting of this canal helps the collateral circulation because arterial spasm is decreased. Simple mechanical release of the artery also aids the circulation. Reports of a few cases with improvement after such an operation are given. J. M. WEAVER, M.D.

The Origin of Postoperative Phlebitis (Le point de départ des phlébites post-opératoires). J. DUCUING, P. GUILHEM, A. ENJALBERT, J. POULHES, and R. BAUX. *Presse méd.*, 1950, 58: 353.

The knowledge of the origin of postoperative phlebitis is not only of theoretic but also of practical importance. One of the authors (J. D.) was able to show that postoperative phlebitis of the lower extremities is frequently preceded by phlebitis of the pelvic veins. Other writers maintain that the process originates in the calf or in the sole of the foot.

Contradictory opinions are due to the fact that the customary technique of phlebography fails to visualize important portions of the pelvic venous system. Therefore, the authors modified the technique by injecting the opaque medium into the dorsal vein of the penis or the clitoris. In this manner Santorini's plexus (its afferent veins and hypogastric veins) can be visualized. The findings corroborated the aforementioned statement that in many instances phlebitis of the lower extremities has its origin in the pelvis. JOSEPH K. NARAT, M.D.

Two Cases of Thorotrastoma with Delayed Clinical Manifestations (A propos de deux cas de thorotrastome à manifestation clinique tardive). J. KUNTZMANN, CH. GROS, and J. MEYER. *J. chir.*, Par., 1950, 66: 201.

Both of the authors' patients were subjected to what was apparently an arteriographic examination with dioxide of thorium (thorotrast). The injections were made by German physicians and it is not known why the examinations were carried out, nor how much thorotrast was used. In both cases roentgen therapy was tried without definite results, and in both there was surprisingly little disturbance of the general bodily function, despite the fact that the examination with the Geiger-Miller counter at the points where the radioactive thorium was deposited disclosed amounts of radiation which were close to the danger line.

One patient complained of edema of the right leg and some vague pains in the abdominal region. Aside from the firm, nonpitting, pigmented edema of the right leg and the palpatory and oscillatory findings of deficient arterial circulation in this extremity, there was an enlarged, firm, and rather painful liver, and, of course, the fist-sized, hard, irregularly contoured tumor (thorotrastoma) in the triangle of Scarpa.

The other patient had been complaining for some months of pain upon flexion and extension of the left knee, of fatigue on walking, and of a frequent sensation of coldness in both feet.

The roentgenographic findings in both cases were in general similar (complete opacification of the liver and spleen) and seemed to involve particularly the reticuloendothelial system. There was some radioactivity in the urine and the histological examination of a biopsy specimen of the liver disclosed deposits of a semicrystalline, shadow-casting material, involving predominantly the Kupffer cells and other tissues of the portal system. These findings indicate, in the authors' opinion, an intense effort on the part of the body to eliminate the toxic material by way of the blood stream and the bile.

In the first patient a subdiaphragmatic sympathectomy was done in an effort to improve the circulation to the extremity. A biopsy specimen from the inguinal thorotrastoma taken at this time revealed the usual picture of an enlarged lymph gland undergoing the changes incident to a chronic inflammatory process (adenoid hyperplasia, reticular hyperplasia, enlarged germinative centers, macrophagia, and sclerotic changes in places).

In the second patient the roentgen examination disclosed, in addition to the extensive thorotrastomatous shadows in the left popliteal region, which had resulted in the cited symptoms, and in addition to an evident atrophic change in the leg, a less extensive involvement of the right leg which had not caused any symptoms.

In neither patient was there any marked change in the condition during the period of observation, and the authors expect none. From their studies in these 2 patients they reach the conclusion that arteriography with thorotrast is contraindicated for any other region than the cerebral cavity. In the latter region not more than 10 cubic centimeters of thorotrast are needed and this amount is probably not too harmful to prohibit its use.

JOHN W. BRENNAN, M.D.

BLOOD; TRANSFUSION

Transfusion Reactions to a Plasma Constituent of Whole Blood. Their Pathogenesis and Treatment by Washed Red Blood Cell Transfusions. WILLIAM DAMESHEK and JACOB NEBER. *Blood*, N.Y. 1950, 6: 129.

Reactions to the transfusion of blood are ordinarily classified as pyrogenic, allergic, or hemolytic. The first two are relatively minor in importance, but hemolytic transfusion reactions, usually due to the use of incompatible blood, are severe and may be lethal.

Another type of reaction to whole blood, not previously described, was observed by the authors in at least 11 cases in the past 3 years. This was characterized clinically by chills, fever, aching sensation in the back and down the legs, and often by a lack of erythrocytic response to the transfusion, although no definite evidence of increased hemolysis was present. Analysis of such reactions demonstrated that they were due to a constituent in the plasma, and could be prevented by the complete removal of plasma from the red cells by thorough washing of the blood with normal saline.

The present report deals with 11 cases showing such reactions to whole blood, subsequently treated successfully with saline-washed red cell transfusions. Evidence of a factor in normal plasma as the cause of the reactions is presented.

During the course of investigating these atypical reactions to whole blood, the value of a simple test which may be described as the "provocative" plasma test was repeatedly demonstrated. The intravenous injection of 20 to 30 c.c. of fresh sterile plasma into patients with the above described abnormal sensitivity resulted in a reaction which occurred either immediately or, at most, within 30 minutes after injection. The plasma used for the test must be freshly separated from recently drawn blood, since stored, heated, or reconstituted dried plasma appears to lack the active component which causes the reactions. The test is simple to perform and harmless. It brings to light the presence of unusual sensitivity to plasma in the recipient, and thus points to the need of transfusing the patient with washed red cells rather than with whole blood.

Although the exact mechanism of these reactions to plasma is not as yet completely clarified, the therapeutic value of washed red blood cell transfusions has become very apparent. In several instances this procedure has been life-saving. In other patients it has enabled the authors to maintain supportive therapy during critical periods in the course of treatment. The possibility of reactions to the plasma in whole blood should be kept in mind in the study of transfusion reactions, particularly if careful investigation by regrouping, repeated cross matching, search for atypical agglutinins, and for hemoglobinuria and hemoglobinemia are negative. This possibility may be confirmed by the plasma provocative test described above. In such cases washed red cell transfusions should prove helpful.

JOHN E. KIRKPATRICK, M.D.

SURGICAL TECHNIQUE

OPERATIVE SURGERY AND TECHNIQUE; POSTOPERATIVE TREATMENT

Use of Blood and Plasma in the Correction of Protein Deficiencies in Surgical Patients. J. Garrott Allen, Willadene Egner, M. B. Brandt, and Dallas B. Phemister. *Ann. Surg.*, 1950, 131: 1.

The authors present the results of a study of nitrogen metabolism in nutritionally depleted patients in whom protein was administered either in the form of plasma or blood to supplement a known oral intake. Various case studies are described in which patients, usually with carcinoma and considerable weight loss, were given plasma or blood (or both) while daily quantitative determinations were done on the blood plasma, nitrogen intake, nitrogen output, and blood volume. The deductions were:

1. Intravenous plasma is utilized more efficiently than intravenous amigen in the correction of plasma deficiency, both with respect to nitrogen balance and elevation of plasma proteins. No latent nitrogen loss was observed with the use of intravenous plasma.

2. It is suggested that intracellular hemoglobin in whole blood transfusions can be utilized for body protein in the depleted patient and that the degree of utilization varies directly as the amount of protein becomes exhausted.

3. Increases in hemoglobin and hematocrit readings were slow and values obtained were less than expected, if all the hemoglobin had been retained in the circulation. This suggests that the body's utilization of hemoglobin for tissue protein may explain why the response to whole blood transfusions is often slow, and indicates the need of further study.

4. Circulatory overloading may occur if care is not exercised in the rate of administration of blood or plasma transfusions, but in general the hazards of undertransfusion are much less than the dangers of moderate overtransfusion.

5. In starvation the concentration of plasma protein and hemoglobin may remain normal for considerable periods of time, because the first change is a reduction in blood volume. If total circulating plasma protein and hemoglobin are calculated, the effects of depletion are detected much earlier.

6. The much more efficient utilization of blood and plasma nutrients, compared to protein hydrolysates, largely offsets the cost differential when blood is donated. C. Frederick Kittle, M.D.

ANTISEPTIC SURGERY; TREATMENT OF WOUNDS AND INFECTIONS

Total Avulsion of the Scalp. Report of a Case. Varaztad H. Kazanjian and Aram Roopenian. *N. England J. M.*, 1950, 242: 539.

The authors report a case of complete avulsion of the scalp from the root of the nose to the nape of the neck, in which the periosteum was intact except for two small areas. The wound had been dressed primarily by a massive wet saline dressing, and although it was contaminated by Escherichia coli, there was no obvious infection. On the third day the area was completely covered by a split-thickness skin graft of four full drums taken by the Padgett dermatome. A few areas which did not take, due to injury to the periosteum, were allowed to epithelialize from the edges. Penicillin, blood, and tetanus antitoxin were given. The patient was discharged from the hospital 6 weeks after the injury and a month later was able to be fitted for a transformation.

The authors stress the importance of the avoidance of contamination, ointments, or escharotics on the primary dressing. The use of antibiotics and early covering of the area by split-thickness grafts are of prime importance.

Thomas C. Douglass, M.D.

Burns from Electricity. G. Kenneth Lewis. *Ann. Surg.*, 1950, 131: 80.

The clinical entity of electrical burns is presented. Low and high tension voltages are differentiated, depending on whether or not the current is less or more than 1,000 volts. The amperage which will affect the human body depends on the bodily resistance, an extremely variable factor. The electrical resistance of the human body has been shown to be less in the elderly, the arteriosclerotic, the alcoholic, the individual with thyroid disturbances, and those with greasy skins. If the body is well insulated and cannot conduct current, it will not be damaged even by high tension voltage. The conditions of contact are important; e.g., whether the current is grasped with a wet or dry hand, etc.

Electrical burns are of two main types: contact and arc. Contact burns vary from pin-point to large surface area lesions; the arc burns result from currents causing an extremely high degree of temperature. Large portions of soft tissues in the region of the wound may separate spontaneously. Any current causes two effects: (1) that of the heat which alters structures along its pathway, and (2) that of the formation of electric sparks which causes third-degree burns at the site of contact.

Frequently with deep burns, the superficial structures appear normal, while the deeper tissues are extensively involved. The original examination will not determine the degree or extent of injury since it is characteristic for these burns to cause alterations of the blood vessels with subsequent thrombosis and necrosis, both of these processes causing changes not apparent for several days or even weeks. Severe hemorrhages may complicate electrical burns.

Tetanic contractions of muscles occur while the current traverses the body; these can be severe enough to tear muscles loose, luxate joints, or frac-

ture bones. Bone lesions are common following necrosis of the periosteum and subsequent sequestration.

The principles of treatment are, first, to disengage the victim from the current, and secondly, to give cardiac stimulation and artificial respiration if these are necessary. The management of the burned area is conservative since the damage to tissue is progressive and may not be completely defined for several weeks. Definitive care will be dependent upon the amount and type of tissue destruction and may necessitate extensive reconstructive surgery.

The author presents 5 illustrative case reports showing the importance of early conservative care and the progressive nature of the tissue damage as contrasted to the initial appearance.

C. Frederick Kittle, M.D.

Parenteral Fluid Therapy. Oscar Bodansky. *Med. Clin. N. America*, 1950, 34: 395.

In this detailed and thorough review, the use of parenteral fluids in terms of deviations from the normal is discussed.

Consideration is given to the normal biochemical structure of the vascular, interstitial, and intracellular components of the body, the deviations from this structure which occur in various diseases and physiological states, and the clinical symptomatology which corresponds to these deviations.

The author points out that even though the administration of parenteral fluids may be guided by certain general principles, therapy must be regulated in accordance with the clinical status and response of the individual patient.

Ely Elliott Lazarus, M.D.

Parenteral Nutrition in the Surgical Patient as Provided from Glucose, Amino Acids, and Alcohol. The Role Played by Alcohol. Carl O. Rice, Burton Orr, and Irving Enquist. *Ann. Surg.*, 1950, 131: 289.

A total of 600 postoperative surgical patients were infused with a mixture of glucose, amino acids, and alcohol. By means of this fluid mixture the patients were provided with their full nutritional and caloric needs.

Calories from alcohol supplied energy for normal metabolism and could be substituted for fat, as proved by the determination of the respiratory quotient. Variations in the blood alcohol level were found to be dependent upon the rate of utilization of the alcohol by the individual subjects. When the blood alcohol level attained a value of .07 per cent to .10 per cent, a sedative and analgesic effect was obtained. The specific dynamic action was estimated at about 7 per cent. It has been suggested that alcohol caused reflex stimulation of insulin secretion and an associated increase in combustion. Alcohol was found to have a protein sparing effect. It was observed that the alcohol mixture was of value in the ready attainment of positive nitrogen balance in surgical patients. The intravenous administration of alcohol caused a rise in gastric acidity, which effect could be suppressed with atropine. Symptoms of intoxication were obtained only on too rapid administration. The incidence of postoperative sequelae, such as ileus, atelectasis, etc., appeared to be reduced because the use of morphine was eliminated. Intravenous alcohol did not cause vomiting, acidosis, or headache.

B. G. P. Shafiroff, M.D.

Finger Infections. K. F. Anderson. *Guy's Hosp. Rep., Lond.*, 1949, 98: 175.

Two hundred and nineteen unselected cases of finger infections in patients seen at Guy's Hospital, London, in 1947, and treated as outpatients were analyzed.

Infections were divided into pulp infections, paronychiae, and superficial infections. Primary treatment consisted of penicillin, immobilization, and "hot soaks," followed by definite incision and drainage. Chronicity occurred in approximately 2 per cent of the patients and was caused by bone involvement, retained foreign bodies, or incomplete drainage. The use of penicillin has brought about a reduction in the average period of disability of patients with pulp infections from 21 days to 9.9 days. Anesthesia was obtained mostly by digital nerve block.

Figures studied permitted the observation that standard therapy, carefully carried out, produced a high percentage of satisfactory results.

Ely Elliott Lazarus, M.D.

The Clinical Importance of Coagulase-Positive, Penicillin-Resistant Staphylococcus Aureus. Paul M. Beigelman and Lowell A. Rantz. *N. England J. M.*, 1950, 242: 353.

The authors demonstrated the penicillin-resistant character of over half of 64 strains of coagulase-positive Staphylococcus aureus. Although penicillin had been used previously in many of the strains, still 20 per cent of the patients had not had penicillin before. Moreover, 30 per cent of the strains were isolated from the noses of healthy children who had never received penicillin. There were 2 cases of sepsis with bacteriemia, in which massive penicillin therapy was inefficacious. It is observed that rapidly developing bacterial resistance to the drug by these organisms will cause failure in therapy. Concurrent administration of other antibiotics may be necessary in overcoming infection by this type of staphylococcus.

Stephen A. Zieman, M.D.

The Noma of Madagascar. A Clinical, Pathogenic, Etiologic, and Therapeutic Study (Le noma de Madagascar. Étude clinique, pathogénique, étiologique et thérapeutique). Boulnois and Rabedaoro. *Sem. hôp. Paris*, 1950, 26: 517.

The noma of Madagascar is a primary nosologic entity; it is not like the noma of Europe, a process secondary to some debilitating general condition (malnutrition, exhausting disease). The process is undoubtedly of an infectious nature. It strikes

mostly young children between the ages of 2 and 5 years, or during the period when the permanent teeth are erupting. The process seems nearly always to strike an otherwise normal, healthy child as an erosion at the neck of the incisor teeth. The infection then spreads down into the bed of the developing permanent tooth, leaving the milk teeth intact. The milk teeth are, however, extruded later, the permanent tooth is destroyed, and the osteitic process then spreads to the surrounding bone of the upper or lower jaw, or both, and in severe cases results in the necrotic destruction of the tissues and bone of a more or less extensive area of the face. After a few days the process ceases to spread, the necrotic soft tissues and bone are cast off, and the child recovers, as a rule, with a monstrous deformity.

Before 1939 the immediate mortality was 80 per cent; however, the medicosocial implications were even worse. An adult with the typical deformation of healed noma of Madagascar has never been seen and it is implied that a child with such a deformity never succeeds in reaching maturity. In 1939 Bouillat and Ramiandrasoa began the treatment of this condition with ascorbic acid and succeeded in reducing the immediate mortality from 80 per cent to 25 per cent. The ascorbic acid also disclosed a startling ability to regenerate the tissues, so that the resultant deformity did not seem to be as bad as when the disease was left to heal of itself. However, despite the powerful curative effects of ascorbic acid, no evidence of relationship of the disease to an ascorbic acid deficiency has been found.

After the introduction of penicillin, the mortality became nil and the only serious problem with the treatment has been one of publicity, propaganda, and finding the cases in the early stages of development. Up to the first of May, 1949, 211 consecutive patients have been treated with the antibiotics at the French Red Cross Hospital of Tananarive without a single death. Of these patients, 148 were treated with penicillin, 51 with tyrothricin, and 12 with streptomycin.

The penicillin was injected into the soft tissues about the necrotic area and into the involved bone, particularly into the affected tooth beds. In addition, this drug was injected intramuscularly in the usual manner and double or triple dosages for the more severe cases. Ascorbic acid, with vitamins A and D_2, is given during the process of healing. If the condition was more advanced when coming under treatment local applications of tyrothricin seemed to have a powerful tissue regenerative effect; nevertheless, many of the children will need plastic repair and the provision of a dental prosthesis to complete the cure.

In the superficial, incipient cases, local applications of tyrothricin were sufficient, and very lately streptomycin was tried and seemed to effect a more rapid recovery than tyrothricin; however, it is enormously more expensive.

In 5 per cent of the authors' material the process started in the mucosa of the cheek region near the buccal commissure but no lesion was observable about the teeth or gums. The lesions were occasionally bilateral and were quite regularly found to begin at about the areas which Stannus demonstrated capillariscopically to be the starting point of the lesions of riboflavin deficiencies. However, no relationship of the process to such deficiencies has been discoverable and the authors are at a loss in explaining the pathogenesis in these cases.

JOHN W. BRENNAN, M.D.

Current Concepts in the Management of Systemic and Local Surgical Infections. JAMES A. DINGWALL. *Surg. Clin. N. America*, 1950, 30: 363.

Wounds subject to infection may be divided into three categories: (1) clean operative wounds which subsequently become infected; (2) wounds accidentally sustained through trauma; (3) wounds resulting neither from trauma nor operative exposure to organisms, but which represent suppuration from introduction of bacteria through minute or unrecognized portals of entry. Examples of this last group would be a felon, a furuncle, or an acute suppurative pyarthrosis. The number of contaminating organisms is minimal in the first group; moderate in the second group, and abetted by dirt and other foreign matter in the wound; and in the third group the infection has often spread beyond the body's natural defenses.

Lockwood has stated that the growth of bacteria in the body frequently depends upon (1) loss of alkaline reserve, (2) the degree of antitryptic power of serum or lymph, and (3) the antibactericidal capacity of the leucocytes. To provide support for healing an infected wound, the patient should be kept in positive fluid balance, and, if possible, in positive nitrogen balance. Blood transfusions and plasma should be administered as needed. Daily recommended dosages of vitamins are: ascorbic acid 1,000 mgm; thiamine, 50 mgm; riboflavin, 50 mgm; and nicotinic acid, 500 mgm.

In all probability the routine preoperative and postoperative use of chemotherapy should be avoided in clean wounds, i.e., in hernioplasty, thyroidectomy, and radical mastectomy. In surgery on the alimentary tract, the preparation of the bowel with one of the enteric sulfonamides, plus streptomycin, is amply justified. Postoperative chemotherapy in these cases is also reasonable.

The presence of known contamination or frank suppuration obviously calls for chemotherapy by an effective and appropriate agent in an effective dose. Cultures should be taken of all infected wounds before chemotherapy is begun, and the sensitivity of organisms to available antibiotics determined. Sound surgical principles should not be neglected because of the wide variety of antibiotics available. In the mixed infections encountered in surgery, two or more antibiotics are frequently more effective than one alone since all currently used antibiotics attack and damage different systems in susceptible bacteria. Tables of effective dosages of sulfona-

mides, streptomycin, penicillin, aureomycin and chloromycetin are included, as well as lists of the organisms against which these antibiotics are usually effective.

In the prophylaxis of tetanus infections, from 600,000 to 1,000,000 units per day of penicillin should be administered plus either a booster dose of toxoid or toxin-antitoxin, 100 units per day, in patients up to 15 years of age, or 1,500 units as an adult dose. In the therapy of tetanus infections, 100,000 units of toxin-antitoxin is given intravenously, plus the same amount intramuscularly. Local lesions may be infiltrated with 10,000 units of toxin-antitoxin daily plus daily intramuscular injections of 10,000 units. Curare is a useful adjunct in controlling muscular spasm. The wound should be débrided of all dead and devitalized tissue and irrigated thoroughly with hydrogen peroxide or zinc peroxide solution. MALCOLM PLUM, M.D.

ANESTHESIA

Peripheral Vascular Homeostasis in Relation to Anesthetic Agents. S. G. HERSHEY and B. W. ZWEIFACH. *Anesthesiology*, 1950, 11: 145.

The authors discuss the effects of anesthetic drugs on specific function of the peripheral circulation. The efficiency of many homeostatic mechanisms may be impaired by age, disease, or by the administration of drugs, the result being that they cannot compensate effectively in stress situations. Some of the anesthetic drugs in common use have been found to modify these homeostatic compensatory patterns unfavorably in the peripheral circulation.

The purpose of the present report is to indicate the extent and direction of some of the alterations affecting the peripheral circulation by the anesthetic agent.

Thirty dogs were anesthetized into the first plane of surgical anesthesia, 10 with cyclopropane, 10 with pentothal, and 10 with ether. A small proportion of omentum was exteriorized and draped over a glass horseshoe in a special moist chamber which served as a stage of the microscope. The blood vessels in the omentum were kept under continuous observation and were photographed at frequent intervals. Graded hemorrhage was utilized as the stress factor to activate circulatory homeostatic responses. The following criteria were employed for evaluation of the functional state of the peripheral circulation: (1) the degree of vasoconstriction, (2) the degree of vasomotion, and (3) evidence of capillary stasis and/or decrease of permeability.

An evaluation of some of the individual mechanisms that additively constitute peripheral circulatory homeostasis has demonstrated striking differences not only between anesthetized and unanesthetized animals, but also in the effects of different anesthetic agents. By means of visual (photographic) methods, the effects of cyclopropane, pentothal, and ether on several homeostatic mechanisms regulating the peripheral vascular bed were compared. On the specific vasomotor mechanisms concerned, cyclopropane exerted little influence, pentothal an intermediate effect, and ether a drastic, unfavorable effect.

The data indicate that anesthetic agents have, of themselves, the capacity to alter the efficiency of some of the homeostatic or compensatory mechanisms of the peripheral circulation.

MARY KARP, M.D.

Circulation of the Air in the Anesthetic Apparatus and in the Respiratory Passages (De la circulation de l'air dans les appareils d'anesthésie et les voies aériennes). MAURICE CARA. *Anesthésie, Par.*, 1950, 7: 21.

The term "controlled respiration" is concerned with manual procedures and apparatus, such as the spiropulsator of Crawfoord, which regulate the respiratory functions of the anesthetized individual. The term "artificial respiration" is concerned with the mechanical function of such machines as those developed by Bernard and by Gréhant, of which the pump and other attachments take care of the ventilating process without the participation of the subject being anesthetized.

Each of the defined types of procedure has its indications. The procedures for controlled respiration, which are more difficult than those for artificial respiration, have certain disadvantages when compared to those for artificial respiration. For example, the uncontrolled amount of ventilation in controlled respiration does not protect the patient against the drying effects of hyperventilation on the bronchial secretions. Thus, the mechanisms with pump attachment would seem to have a brighter future than those which control the respiration automatically, especially for the major operations on the heart and lungs. Controlled respiration would, of course, still subsist for the minor operations and for emergencies.

The closed circuit apparatus with pump attachment for artificial respiration is, of course, more cumbersome; however, there is no reason why such an apparatus could not be constructed with a firm base, perhaps in a room adjoining the operating room, and be operated from such adjoining room.

For minor surgical interventions the natural powers of respiration of the patient would seem to be most advantageous, since they would avoid the possibility of hyperventilation. If the smaller and lighter, to-and-fro apparatuses for controlled respiration, with their (on the whole) inefficient removal of the carbon dioxide from the utilized gases by means of calcium lime (CaO) (instead of being bubbled through a tank of potash solution as in the machines of Krogh and of Knipping) be used, means of efficient aspiration of the inspissated bronchial secretions should always be at the disposal of the anesthetist.

In the construction of the anesthetizing apparatus the chief problem is one of ventilation, that is, the circulation of the air within the respiratory passages of the patient and within the apparatus itself. The

motion of ventilation, which may be calculated as the product of the respiratory frequency and the volume of the air stream, is what is to be kept in view in studying the intensity of the circulation of gases or in calculating their resistances. In the solution of this problem reference must be made to all that we know concerning the physiology and the mechanical laws (Poiseuille, Reynolds, Venturi) governing respiration. JOHN W. BRENNAN, M.D.

Experimental and Clinical Investigation of Two New Analgesics During Nitrous Oxide Anesthesia. Preliminary Report. RICHARD C. THOMPSON and WILLIAM B. NEFF. *Current Res. Anesth.*, 1950, 29: 77.

This article is concerned mainly with the efficacy of two new agents, bemidone and ketobemidone, to supplement the pain-relieving qualities of nitrous oxide anesthesia. The effects of the new analgesics, which are piperidine derivatives resembling demerol, were studied on dogs and humans and compared with the effects of morphine and demerol.

The analgesic activity of bemidone appears to be twice that of demerol, but certain undesirable side reactions render it less suitable than demerol. It caused a pronounced decrease in respiratory amplitude, hyperexcitability, and some alteration in the peripheral circulation.

The keto-compound is a potent analgesic and respiratory depressant; it is fifteen to twenty times more powerful than demerol, with which it compares favorably as an adjunct to nitrous oxide and oxygen anesthesia.

The undesirable effects on respiration and circulation of each of the compounds is minimized by the slow injection of dilute solution. Dryness of the mouth, mild relaxation, and drowsiness were noted with each drug. Neither produced euphoria.

MARY FRANCES POE, M.D.

Evipal Sodium—d-Tubocurarine Chloride for Endotracheal Intubation: Preliminary Study. PERRY P. VOLPITTO and CHARLES C. BENTON. *Anesthesiology*, 1950, 11: 164.

A technique is described for the intravenous administration of sodium evipal d-tubocurarine chloride for endotracheal intubation. The authors have used this method for intubation of 118 patients. A report of 100 additional cases in which the method has been employed is appended. This technique has now assumed a routine status for all intubations in the institution. The authors believe that the occurrence of severe stridor or laryngospasm has been less in this group as compared with those intubated under sodium pentothal and curare.

A 5 per cent solution of evipal sodium was found optimal. Fifteen milligrams of high potency d-tubocurarine chloride was added to 9 c.c. (½ gm.) of evipal solution, each cubic centimeter of the mixture containing 50 mgm. of evipal and 1.5 mgm. of d-tubocurarine chloride; 5 c.c. are given as an initial test dose and further additions depend upon the presence of varying degrees of respiratory depression. The object is to obtain deep narcosis of the patient and relaxation of the masseters and laryngeal muscles. Actual anesthesia is not necessary.

The Macintosh laryngoscope blade has been found to facilitate vision of the larynx and the intubation.

The ages of the patients ranged from 5 years to 82 years, and the dosages ranged from 8 to 16 c.c. A policy was established early, not to exceed a dose of 10 c.c. of the combination of agents (500 c.c. of evipal and 15 mgm. of d-tubocurarine). No serious complications occurred in the present series of cases. Relaxation of the masseter and pharyngeal muscles was not adequate in 12 per cent of the patients. Recovery of the patient was rapid. After intubation, anesthesia was continued with gas ether.

MARY KARP, M.D.

Intravenous Anesthesia with Dolantin and Evipal Sodium Combined (Die intravenoese Dolantin-Evipan-Na-Narkose). ARNOLD HOFMANN. *Chirurg*, 1950, 21: 65.

Although intravenous anesthesia with evipal sodium is quite satisfactory for operations of short duration, it has certain disadvantages. The most important of these are: (1) a fine tremor, which sometimes interferes with the work of the surgeon, (2) singultus, especially when the stomach or duodenum are manipulated, and (3) postoperative excitation.

The author developed a new intravenous method in which evipal is combined with dolantin. He reports excellent results with this type of anesthesia. Dolantin, manufactured by Bayer in Germany, is 1-methyl-4-phenylpiperidin-4-carbonic acid ethyl ester; it has spasmolytic as well as analgesic properties. In addition, it reduces salivation and suppresses the cough reflex.

The technique is the following: 100 mgm. (2 c.c.) of dolantin are slowly injected into the vein; then with the needle left in place, evipal is injected from a different syringe after an interval of 3 minutes.

This combination method has been tested in a series of 500 cases. It obviates the mentioned disadvantages of pure evipal anesthesia and reduces the necessary amount of evipal by about 25 per cent. No premedication with morphine or atropine is necessary.

The only contraindications are severe shock and liver damage. No untoward side effects were observed. WERNER M. SOLMITZ, M.D.

Intravenous Procaine—An Adjuvant to General Anesthesia: A Preliminary Report. IVAN B. TAYLOR, ALEXANDER B. STEARNS, HARRY C. KURTZ, JOHN C. HENDERSON, and Others. *Anesthesiology*, 1950, 11: 185.

The authors present the results which they obtained in 211 administrations of procaine hydrochloride intravenously during general anesthesia. Procaine given intravenously at rates of from 10 to 60 mgm. per minute seems to be helpful in depressing

some of the activity of the autonomic nervous system. It also furnishes analgesia, and depresses cough and pain reflexes; its action is not absolute but of a depressing nature that is frequently helpful during and after general anesthesia and its use has been found most valuable in anesthesia for thoracic, thyroid, and cardiac surgery.

The technique used has been fairly consistent. One per cent procaine hydrochloride in 5 per cent glucose solution is the agent of choice. General anesthesia is induced with the drug of choice, usually pentothal with or without curare. Intravenous procaine is started at 40 mgm. (4 c.c. of 1 per cent solution) per minute in the average adult.

Certain observations have been made:

1. Cough reflex is depressed enough so that an endotracheal airway can be tolerated without coughing during very light anesthesia.
2. Cardiac arrhythmias have been prevented with the use of procaine during intrathoracic operations with cyclopropane.
3. Sweating is depressed.
4. The entire respiratory tract is usually very dry and emergence nausea and retching are absent.
5. Recovery is quiet and rapid.
6. Postoperative analgesia may last for 20 minutes to several hours.
7. Intravenous procaine is helpful in maintaining light anesthesia with any general anesthetic drug.

Some of the dangers and disadvantages of using this agent are circulatory depression, muscle twitching, and respiratory arrest which occurs at about the same time as circulatory cessation. Sensitivity to the drug and delayed reaction may exist, but have not been encountered in this series. An experienced anesthesiologist is essential to the use of the method.

MARY KARP, M.D.

SURGICAL INSTRUMENTS AND APPARATUS

Synthetic Adhesives—A New Hemostatic Agent. A Third Report. M. LESTER LOWRY. *Arch. Surg.*, 1950, 60: 793.

An extensive investigation of many colloid adhesive compounds was undertaken. The hemostatic effectiveness of each of these solutions was checked by topical application to the freshly cut surfaces of the liver of white rats. A compound of polyvinyl alcohol, sucrose, and urea proved to be the most effective hemostatic agent, and these compounds were demonstrated to be nonirritant to the tissues.

F. J. LESEMANN, JR., M.D.

Fundamentals of the Procedure of Thermoelectric Measurement of the Temperature, Especially in Surgical Interventions (Grundsaetzliches zum Verfahren der thermoelektrischen Temperaturmessung, insbesondere bei chirurgischen Eingriffen). H. EIERMANN and H. H. MICHLER. *Chirurg.*, 1950, 21: 12.

The authors discuss the procedure of thermoelectric measurement of the temperature and its advantages, but warn against sources of error. Although the thermoelements can be made very small, their introduction into the body constitutes quite an annoyance for the patient; therefore, the physician will try as much as possible to make the measurements on the body surface. However, in doing this he should be very careful since small changes in the coverings of the site of measurement, or in the room temperature when the site is uncovered, may lead to marked changes in the surface temperature. In some cases of serial measurements during surgical interventions, abnormally high temperatures were noted which exceeded the coagulation point of albumin and could not have originated physiologically; it was found that these erroneous measurements were due to the use of a thermocautery during the operation. This experience should be of great interest for neurosurgery in which nearly all interventions are carried out with this instrument.

To carry off the high frequency current without damage to the patient and yet to be able to use small thermoelements, the authors experimented with a ball element 1 mm. in diameter surrounded by a grounded protective ring 50 mm. in diameter and connected the thermoelement with it through a short wire. The diathermic action on this greatly enlarged surface still produced an excess temperature of from 1° to 2° C. on the left plantar surface. The slow cooling off of the tissues under the protective ring made exact measurements of temperature impossible for a long time after thermocauterization.

Errors in measurement can also be caused by the thermoelements themselves. The repeated insertion and disinfection of the needles may cause defects or interruptions in their isolation with consequent variations in the readings. Also, the needles gradually become blunt from continued use and must be sharpened; this may change the element and result in errors up to 1.5° C. On the other hand, new elements show aging in the beginning, which is probably caused by metallurgic changes; this necessitates verification of the gauge after a time during which the elements should not be used for precision measurements. The aging process may be shortened by frequent heating and cooling.

Unless these factors are given due consideration, the results of thermoelectric measurements during operations must be taken with a grain of salt. In fact, when the thermocautery is used on the intestine or inside of the skull, it is more to the point to accept an increase in the temperature of cutaneous sites as a result of the high frequency current than attribute it to disturbances of the sympathetic system or of central regulation. RICHARD KEMEL, M.D.

Nitrogen Metabolism after Surgical Operations. Use of a Protein Hydrolysate after Partial Gastrectomy. A. M. WILKINSON, BARBARA H. BILLING, GABRIELLA NAGY, and C. P. STEWART. *Lancet*, Lond., 1950, 1: 533.

Since 1939 there have been numerous reports on the administration of protein hydrolysates before

and after major surgical operations. Among other claims made for these preparations, it was said that with their aid the increased catabolism of protein which regularly follows injury could be largely or entirely prevented. This claim seemed to be unproven, but in some circumstances prevention of the postoperative loss of nitrogen would clearly be of great advantage. In 1946 the Protein Requirements Committee of the Medical Research Council proposed that the value of such hydrolysate therapy should be investigated and invited the authors to take part in the investigation. The following report embodies some of the results obtained in clinical trials on surgical patients.

The investigation on well nourished patients who had undergone partial gastrectomy has shown that an increased urinary nitrogen excretion begins on the second day after operation and lasts from 5 to 8 days, the greatest loss being between the second and fifth days. This increase in urinary nitrogen can be resolved into three fractions: (1) due to starvation for protein; (2) due to the restriction of caloric intake; and (3) a major fraction related in some way to the operative injury. This third fraction seems also to be related directly to the initial total mass of body protein, which in turn is governed by the preceding state of protein nutrition together with factors such as previous disease.

That some part of the "catabolic phase" is due to injury and the subsequent recovery process is strongly suggested by its constant occurrence in well nourished patients, irrespective of the food intake during the immediate postoperative period. The excessive breakdown of protein which constitutes the catabolic phase, and is shown by an increased urinary nitrogen excretion rather than by a negative nitrogen balance, has been found after injury and disease of the most varied kinds and in species other than man; it is not abolished by the intake of protein, even when the protein is adequately protected by carbohydrate, and is much less evident or even absent in undernourished persons with little or no protein available for catabolism. These considerations inevitably raise the question of whether the catabolic phase is a pathologic phenomenon to be combated by forced feeding or whether it constitutes a fundamental biological reaction to injury. In the latter case it should be considered that the catabolic phase may even be a valuable reaction and ought not to be interfered with; at least it is associated in time with reparative activity, it appears to do no harm, and it cannot be abolished by normal feeding methods.

The administration of protein (as such) or of protein hydrolysate intravenously merely increases the urinary nitrogen proportionately and does not modify the "catabolic phase" in any essential way.

This increased urinary excretion does not occur in persons who are deprived of food protein but do not undergo surgical operation.

There is a negative nitrogen balance during the postoperative period, irrespective of the protein intake, and in persons who receive little or no protein but are not submitted to surgical operation.

Hence the postoperative change in protein metabolism is due partly to the usual reduction in food intake and partly to an increased protein catabolism which is inseparably associated with injury. The latter factor, the important part of the "catabolic phase," is most clearly demonstrated by the postoperative increase in urinary nitrogen rather than by the negative nitrogen balance.

BENJAMIN GOLDMAN, M.D.

PHYSICOCHEMICAL METHODS IN SURGERY

ROENTGENOLOGY

Air Myelography in Herniated Intervertebral Disc (Die Luftmyelographie beim Bandscheibenprolaps). J. BUECKER. *Fortsch. Roentgenstrahl.*, 1950, 72: 493.

The author carried out air myelography on 60 patients in whom a clinical diagnosis of herniated intervertebral disc had been made and obtained unequivocal positive findings of herniated disc in 6 of them. The findings were confirmed by operation in 5 patients. The sixth patient was not operated upon.

The patients were placed in a lateral position on a Bucky table with the foot of the table elevated about 30 degrees, and from 50 to 60 c.c. of fluid were withdrawn and replaced with about 50 c.c. of air. At the lumbosacral junction the author did not observe an air column of diagnostic value. Only lateral or somewhat oblique views showed the air-filled canal distinctly. Sagittal views were of no definite value even in cases of gross prolapse. Illustrations of roentgen views are presented in the original article which demonstrate distinct narrowing of the air column by disc protrusion. Only the more gross protrusions could be positively demonstrated by air myelography. Smaller prolapses, especially when they lay laterally, and circumscribed thickening of the ligamentum flavum could not be demonstrated.

In order to achieve visualization, general conditions must be favorable. Obesity, heavy musculature, a large transverse diameter, and superimposition of the pelvic bones can obliterate the contrast necessary for diagnosis. The value of air myelography is limited, but in the absence of a completely harmless positive contrast medium it may prove of assistance in diagnosis and in the plan of operation.

JOHN L. LINDQUIST, M.D.

Epidermoid Tumors of the Cranial Bones and Vertebral Canal, with Particular Reference to Roentgen Findings (Epidermoide des Schaedelknochens und Wirbelkanals unter besonderer Beruecksichtigung der Roentgenbefunde). WALTER DUEBEN. *Fortsch. Roentgenstrahl.*, 1950, 72: 484.

The author reports 2 cases of epidermoid tumor involving the cranial bones and 3 cases of pearl tumor of the vertebral canal, with emphasis on the roentgen findings. A presumptive diagnosis of these tumors can be made with a high degree of probability prior to operation on the finding of roentgen changes. In the skull these changes consist of raised up and honeycombed areas of decalcification which are sharply demarcated by a narrow, smooth zone of increased calcification. In the vertebral canal the changes consist of a smooth, marginal indentation or excavation of several vertebral bodies demarcated by a narrow zone of sclerosis.

Roentgen study of 2 of the cases involving the spinal canal with an intramedullary and intradural location failed to reveal any bone change.

JOHN L. LINDQUIST, M.D.

A Contribution to the Roentgenological and Clinical Aspects of Fetal Hypophyseal Adenoma (Ein Beitrag zur Roentgenologie und Klinik des foetalen Hypophysenadenoms). L. PSENNER. *Fortsch. Roentgenstrahl.*, 1950, 72: 586.

The case here reported was that of a 35 year old woman who had been suffering for a year from diminishing vision, headaches, pains in the eyes, dizziness, and vomiting, and who at present exhibited a homonymous quadrant hemianopsia and central scotoma in the right eye.

The roentgen examination disclosed a cranial vault which appeared normal in respect to form, size, and structure. There was no evidence of increased intracranial pressure. The base of the skull, however, exhibited extensive changes. The sella turcica, with inclusion of the tuberculum and sulcus chiasmatis was completely destroyed. The destructive process had also extended to the neighboring portion of the body of the sphenoid; the sphenoid sinus, on lateral exposure, appeared as a narrow cleft, showing a soft tissue shadow. The verticosubmental exposure disclosed a sphenoid sinus of which the anterior wall and the anterior portion of its cavity were entirely normal and empty of any evidence of abnormal content. The posterior wall, however, had undergone pressure atrophy and the tumor shadow had protruded forward into the sinus cavity so as to fill its lumen two-thirds full. The anterior clinoid processes were shortened, running to sharp points, and they appeared to be elevated.

At operation a large tumor was uncovered. It had elevated and pressed flat the optic nerves and extended as far forward as the angle of the chiasma. The neoplasm was evidently extremely vascular and evidently not removable. A biopsy specimen from the tumor was pronounced fetal hypophyseal adenoma. Following the operation the patient began to menstruate again. From this it is deduced that the anterior lobe of the hypophysis was still present and had been freed from pressure by the operation.

The author wishes hereby to direct attention to the value of roentgenology in these tumors of the hypophyseal region, particularly in the matter of differentiating between malignancy and benignancy. The tumor here reported was adjudged to be a benign one from the fact that it merely pushed the mucosa of the posterior wall of the cavity forward without obliterating the cavity of the sinus by the reactive swelling which characterizes the mucosa when infiltrated by cancer cells. Excision and histological examination of the biopsy specimen procured from the region here concerned will lead to

more or less certainty as to the nature of the tumor present, but will reveal nothing of its benign or malignant nature. This limitation is due to the fact that, as a rule, in the tumors of the region of the sella turcica, the region of contact of the neoplasm with the normal tissues is not included in the biopsy specimen, and it is along this border region that the processes of malignant infiltration are evident.

The fetal hypophyseal adenoma, characterized by immature, undifferentiated cells (which are the exact counterparts of the cells of the hypophyseal gland during fetal life), is to be regarded as a benign growth. The tradition of its malignancy has arisen from its analogy to the fetal adenoma of the thyroid gland which occasionally disports malignant tendencies.

With reference to the point of origin of this tumor, it is concluded that in all likelihood it is intrasellar; although the possibility of an origin elsewhere, for example, within the body of the sphenoid bone, cannot, of course, be excluded.

JOHN W. BRENNAN, M.D.

The Contribution of Roentgenology to the Diagnosis of Primitive Cancer of the Lung (Il contributo della radiologia alla diagnosi del cancro primitivo del polmone). FELICE PERUSSIA. *Rass. internaz. clin. ter.*, 1950, 30: 65.

Pulmonary cancer demands attention because of its increasing frequency, not only as a clinical entity, but also at the autopsy table, and because the recent acquisitions of the surgeon, such as the new methods of anesthesia, the advent of the antibiotics, and the new techniques of intrathoracic surgery itself render an early diagnosis imperative. The operation (pneumectomy) must be performed before the tumor growth has reached the point of producing atelectasis, inflammatory infiltration, colliquative changes, carcinomatous lymphangitis, or metastases in the mediastinal lymph glands.

The precocious recognition of the pathology present is especially difficult and uncertain for the reason that cancer of the lung in its early stages is so apt to be silent. Vague pains in the chest, a stubborn cough, a little coughing of blood are sufficient to arouse the suspicion of cancer and to indicate, indeed to demand, all the resources at present obtainable to clarify the nature of the complaint.

The bronchoscope will permit the obtaining of secretions for cytologic study, or of a biopsy specimen; however, this should not complete the examination. The teleroentgenogram at different angles should be added, stratigraphy and bronchography should be practiced, and in their collective results will often permit of a preciseness of diagnosis not otherwise obtainable.

About 90 per cent of pulmonary cancers involve the larger air passages; the remaining 10 per cent, therefore, are located peripherally and perhaps even subpleurally. In the latter location they may be out of reach of every other method than that of roentgenology, and even with this method the roentgen ray—even when used in the stratigraphic technique—may present confusing appearances. The fibrosclerotic form of pulmonary cancer growth, which has been given the designation of Assmann infiltration, practically cannot be differentiated roentgenologically from fibrocaseous ulcerative pulmonary tuberculosis.

The stratigraphic method can be used to elineate the solid neoplastic core in a less deeply shadowed field consisting of edema, atelectasis, or pleural effusion. The stratigraphic roentgen examination will furnish information about the extension, structure, and relationships with the bronchi and blood vessels of the tumor mass. The method will be found most important in determining the existence of metastatic glands of the hilus or mediastinum. Nevertheless, the stratigraphic method requires enormous experience for the proper interpretation of results. But few lesions, even of the large air passages, run transversely to the plane of sight. Most of them are caught in an oblique direction and even at the point of sudden change of direction. Such findings are liable to be interpreted as stenosis.

The angular bronchoscope will now permit a view of the bronchi leading to the upper lobes, but will not permit of taking the biopsy specimen. Bronchography permits of examination of conditions at a greater distance peripherally than the bronchoscope. It does not easily distinguish between the different forms of obstruction (spasm, blood coagula, secretions, etc.); nevertheless it will show absence of bronchoalveolar injection, deviations of the bronchial tree, and bronchiectasis.

The thing for which the surgeon must always be looking is the growing neoplastic nodule with its mamelonated border, so different from the rounded or oval cysts and the irregular borders of tuberculosis. Even in advanced cases with cavitation, abscess formation, and the feverish, wasting symptoms of tuberculosis, such solid core with polycyclic (hilar lymph glands) or mamelonated, sharply delineated borders will at times uncover the neoplastic origin of a process which therwise is characteristic of tuberculosis.

JOHN W. BRENNAN, M.D.

The Roentgen Cinematographic Apparatus and Technique for Visualizing the Heart Cavities and the Large Vessels. Angiocardiocinematography (Apparatur und Technik der Roentgenkinematographie zur Darstellung der Herzbinnenraeume und der grossen Gefaesse. Angiokardio-Kinematographie). R. JANKER. *Fortsch. Roentgenstrahl.*, 1950, 72: 513.

Eleven photographic reproductions of the machine in parts and in use, in the original text, give an adequate idea of the general manner in which the apparatus under discussion is constructed. The remaining photograph (Fig. 1) reproduces some of the serial film portrayals in a case of the tetralogy of Fallot in a 9 year old girl. The roentgen cinematographic study in this case enabled the heart surgeon to determine the side on which the operation had to

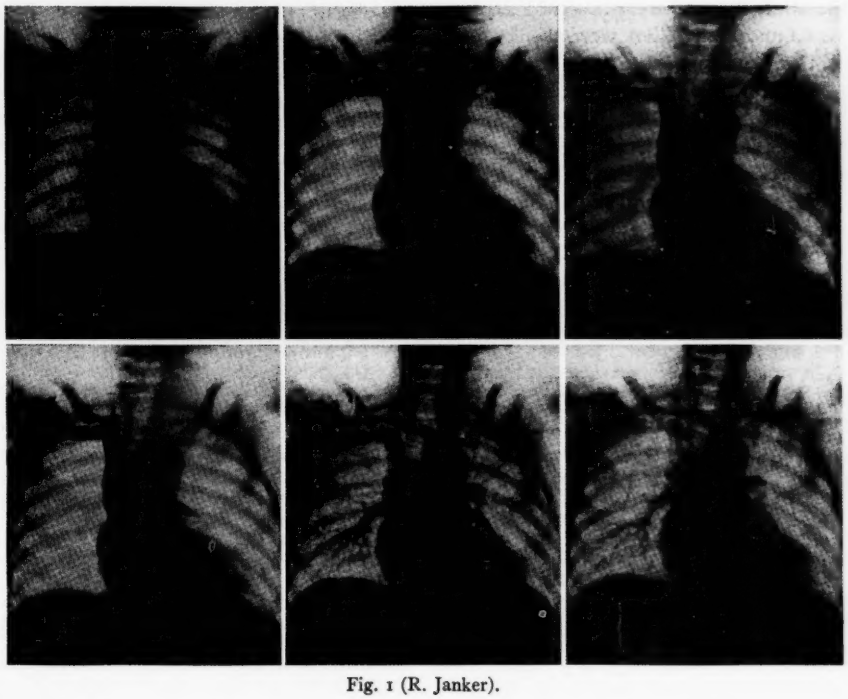


Fig. 1 (R. Janker).

be done and led to a successful conclusion of the operation itself.

The patient lies on the table surface in which is set the fluoroscopic screen. The roentgen rays pass from above through the heart region of the patient to the screen. The image produced on the screen is then reflected from below by a mirror set at 45 degrees into a special movie camera, constructed from the author's specifications. The camera may be moved toward or away from the mirror so as to procure a larger or smaller field, respectively.

The radiation output from the roentgen tube, which is filtered by 1 mm. of aluminum, is centered carefully in order to spare the skin of as much of the injurious radiation as possible. The problem of possible skin injury in this work is a real one. The radiation burden by the skin in the 6 to 8 seconds of exposure with 65 cm. focal distance, with the necessary 90 kv. and 80 ma., in order to get clear pictures is exactly 50 roentgens. However, a mechanism has been developed wherewith the current to the tube can be cut off except for the exact time of taking each successive picture. This cuts down the skin load by 25 per cent. The mechanism takes advantage of the afterglow of the fluoroscopic screen which continues for a brief period after the ray has ceased passing.

The operating personnel had, of course, to be protected also. This, in the author's opinion, has been adequately done. An arrangement of lead-lined screens and walls with leaded glass (equal to 2 mm. of lead lining) peepholes enable not only the entire process of photography to be watched but also the supervision and performance of passing the heart catheter in the cases in which this maneuver is considered necessary.

The contrast substance employed is either 30 per cent ioduron or 35 per cent perabrodil. According to the size, age, and robustness of the patient and the nature of the clinical condition present, the amount of these substances used is usually from 30 to 60 c.c. Before the substance is used, of course, the patient is tested for local (intracutaneous injection) and general (intravenous injection) sensitization. Other than a mild sedative, no form of anesthesia is now used for any stage of the procedure. If the patient shows no reaction to a 1 c.c. intravenous injection it is assumed that he is not sensitized. However, oxygen and suprarenin solution (1 to 1,000) are kept handy to combat possible shock. The patient is fasting when coming to the table for the angiocardiography.

The side reactions noted have been a heart stop for a few seconds, irritative cough, vomiting, headache, depression, a slight drop in the blood pressure, and a moderate grade of cyanosis. These manifestations, however, disappear in a few minutes under the

administration of oxygen. Following the examination, from 400,000 to 600,000 units of penicillin are given in a period of 2 days.

In spite of repeated examination with this method many of the details of the heart and vascular movements are still not fully explained. A still greater number of pictures per second is necessary. Therefore, while waiting until this possibility becomes a fact, the author has devised a copying-apparatus which enables a "stretching" of the time interval. Two copying apparatuscs are so adjusted together that the negative strip courses in the one, and the positive strip in the other. The copying can be so chosen then that each tiny negative image is individually reproduced. However, each of the negative images can remain longer in the window and in this manner be copied one after the other for 5, 10, or 20 times. The process is thus stretched out from 5 to 20 times. By this means it is possible to "stretch" extremely rapid movements frequently occurring in a fraction of a second, and more easily analyze them.

At present efforts are being made to produce a roentgen cinematographic exposure in 2 planes in order to produce a stereoscopic effect.

JOHN W. BRENNAN, M.D.

Retropneumoperitoneum. A New Method of Roentgenologic Exploration of the Abdomen. (Le retropneumoperitoine. Nouveau procédé d'exploration radiologique de l'abdomen). L. DE GENNES, J. P. MAY, and G. SIMON. *Presse méd.*, 1950, 58: 351.

Large amounts of gas, frequently required for visualization of the liver or spleen, when pneumoperitoneum is employed, are apt to provoke severe abdominal pain, dyspnea, or syncope. Due to a slow diffusion of the gas, it is difficult to obtain a clear picture of the kidneys.

On the other hand, the pneumorenal insufflation introduced by Rosenstein furnishes much better images of the kidneys and the suprarenal glands, but a very exact technique is required; pain is not infrequently provoked, and various complications such as hemorrhage, gas embolism, and even a fatal outcome may follow.

Rivas, in 1947, showed that following a spinal extradural injection of air, the subdiaphragmatic region could be visualized.

The authors employ the following technique:

Oxygen is used for injections, but carbon dioxide or an equal mixture of both gases probably serves the purpose just as well. An apparatus that allows control of the pressure and the volume of gas must be used. Enemas are given the night before the study. The patient receives a subcutaneous injection of prostigmin and is placed in a knee-chest position. A 4 cm. long needle, connected with the gas tank, is introduced under aseptic conditions 1 cm. from the coccyx in the anococcygeal line. Gas is introduced above the anococcygeal raphe under pressure of 300 gm. From 1,000 to 1,200 c.c. of oxygen are injected within 3 minutes. Perineal emphysema, recognizable by crepitus, must be avoided. After the injection the patient is placed in a semi-sitting position. After a period of 1 hour he assumes a supine position and pictures are taken. The best roentgenograms are obtained 2 hours after the injection. Accidental puncture of the rectum can be avoided by employment of a needle not longer than 4 cm. Many patients complain of slight pain in the left iliac fossa, which disappears spontaneously within 20 to 30 minutes. No serious complications have been observed.

The following organs are visualized: the psoas muscles, the diaphragm, the kidneys, the suprarenal capsule, the spleen, and the liver.

JOSEPH K. NARAT, M.D.

Diagnostic Pneumoperitoneum in the Roentgenologic Investigation of the Left Hypochondrium (Il pneumoperitoneo diagnostico nell' indagine radiologica dell'ipocondrio sinistro). R. CAMERINI and L. GUARDABASSI. *Arch. ital. mal. app. diger.*, 1950, 16: 3.

The solution of the roentgen diagnostic problem in the left hypochondrium requires first of all an accurate physicogeometrical evaluation of the obtained images because the pneumoperitoneum creates artificial contrast lines between the introduced gas and the contours of the various organs. Another important element is the degree of possible displacement and reciprocal separation of the viscera; the uncertainty of the normal picture makes the interpretation of many elements rather difficult. An important factor for the visibility of the organs may be the presence or absence of gas in the posterior epiploic cavity. In addition, thin layers of gas may obliterate completely, or nearly completely, thick visceral layers or intense visceral opacities, so that artificial pictures with decided contrasts or formations with clear-cut contours, not corresponding to real anatomic formations, may result from the volume and disposition of adjacent or overlying gas; therefore, estimation of the thickness of organs on the basis of the degree of opacity is very unreliable. Particularly interesting is the possibility of the formation of long, thin hyperilluminated and hypoilluminated lines in connection with the phenomena noted in so-called total reflection. Thus, the acceptance of an abnormality in form, seat, and relations of an organ presupposes the exclusion of all purely physical factors which may be responsible for a roentgen abnormality in an anatomic normality; this is the most difficult thing to do and is the greatest source of diagnostic errors.

To study the superoexternal curve of the hypochondrium, the best position of the patient is the erect one with anteroposterior or posteroanterior and right lateral projection, and the supine or prone position with laterolateral incidence for the anterior and posterior surface. In most cases the course of the curve is regular and continuous, but it may present a segmental undulation prevalent in its upper part, a festoonlike double line, a Y bifurcation, and nodular, lamellar, isolated, or diffuse irregularities.

The thickness of the diaphragmatic arch may be above normal because of pleural thickening or effusion over the entire arch or part of it. When it is impossible to find a thin semilunar layer of gas underneath the diaphragm, there is no reason for making immediately the diagnosis of total splenophrenic or hepatophrenic adhesion, particularly if the presence of even a small quantity of peritoneal fluid cannot be excluded; in fact, the splenic convexity may remain against the diaphragm without the existence of organized adhesions.

Visualization of the thickness of the gastric wall is not always easy; this wall appears as a semiopaque streak directed outward and downward, from 3 to 5 mm. thick, delimited externally by the peritoneal gas and internally by the gastric gas, and presenting a slightly wavy and irregular course internally because of the mucosal folds. Median displacement of the liver and spleen by the pneumoperitoneum may superimpose the left portion of the small hepatic lobe on the spleen and simulate splenomegaly or a pathologic mass in the left hypochondrium. The superoexternal border of the spleen is easily recognized. The presence of nodosities on the great splenic curve, sometimes with polycyclic aspect, is found in cysts, metastases, or abscesses; isolated nodosities are rarely due to echinococcosis; the upper pole may be pointed, ogival, or ovoid; the lower pole is usually delimited by the phrenocolic ligament on which it rests. An important distinctive sign of the anteromedian border is the splenic incisure which is sometimes visible only in oblique exposures and rather rarely in splenomegaly and hepatomegaly. The possibility of a change in the seat, form, and size of the spleen must be considered. Roentgen examination is of little help in the interpretation of the causes of splenomegaly; the relations between the volume, consistency, and change in form under pressure and decubitus are more useful. It is rarely possible to visualize the middle portion and the tail of the pancreas. The examiner should not forget that an apparent agreement between clinical and roentgen findings may be as deceptive as a discordance. RICHARD KEMEL, M.D.

An Illustrative Case of Gastritis Polyposa (Kasuistischer Beitrag zur Gastritis polyposa). ERNST EIBACH. *Fortsch. Roentgenstrahl.*, 1950, 72: 573.

The differentiation of the benign hyperplastic manifestations of the stomach from the malignant processes is one of the most difficult and frequently insoluble problems of clinical medicine. The relationships of anemia, gastritis, and tumor of the stomach have likewise been the object of much study. The present case should therefore be of interest in that the process has seldom been reported in the form of such an enormous development.

The patient was a 56 year old male whose brother, older by 10 years, was also under care for cancer of the rectum. The polypous condition had first been diagnosed 2 years before. At the time of the present examination there was palpable and visible the transversely directed cylindrical tumor across the epigastrium. The mass was smooth, rather soft in consistency, and apparently notched along the lower border. There was no blood in the stool. A histamin-refractory achylia was encountered.

The roentgen examination showed coarse defects in the gastric shadow, especially along the greater curvature. These defects demonstrated finger-thick rolls of hyperplastic stomach mucosa which under graduated pressure failed to show any of the fine mucosal definition of the normal stomach lining. The pyloric canal was lengthened and there was a defect on the side of the greater curvature in the pyloric contour. Peristalsis was slight, but nowhere was it entirely absent. The stomach always emptied itself of the shadow mixture within 3 hours.

A year later the patient came in for a recheck. He had increased in body weight, the palpatory findings were the same, and he still gave evidence of a mild grade of secondary anemia. At this time the gastric relief picture was practically unaltered. The finger-thick polypoid masses were still present and a complete filling of the stomach with the shadow material showed a marked grade of gastric ectasia.

Four months later the patient came back again. The gastric and blood findings were practically unaltered; however, he had again put on some weight. In none of the roentgenograms was there ever any abnormality in the remainder of the gastrointestinal tract.

Thus, in an observation period of almost 3 years the hyperplastic polypoid condition of the stomach was able to produce a mild grade of secondary anemia, but showed no tendency toward malignant degenerative change. JOHN W. BRENNAN, M.D.

A Study of the Roentgenologic Findings in Ulcerative Tumors of the Stomach (Considerazioni sul reperto radiologico in tumori ulcerati dello stomaco). FAUSTO CESARANI. *Radiol. med.*, Milano, 1950, 36: 97.

The fact is emphasized that in many instances a clinical, laboratory or single roentgenologic examination does not permit differentiation of a benign ulcer from a malignant lesion on the lesser curvature of the stomach, especially in the prepyloric region. It is estimated that about 75 per cent of all gastric cancers are located in the antropyloric region.

X-ray studies repeated at regular intervals are essential for the diagnosis.

Reduction of the size of the niche does not necessarily speak against the malignant character of the lesion.

A coagulum, food particles, or perigastritis may be responsible for irregular outlines of the niche caused by a benign ulcer. Hence, this feature cannot be considered characteristic for malignant ulceration.

Likewise, convergence of gastric plicae toward a benign ulcer and their sudden interruption at a malignant ulcer are not reliable diagnostic criteria.

The size of the niche is of no great value for differential diagnosis, as very large niches caused by benign lesions have been described.

JOSEPH K. NARAT, M.D.

Roentgenologic Diagnosis of Inflammatory Diseases of the Small Intestine (Roentgendiagnostik der entzuendlichen Duenndarmerkrankungen). R. PRÉVÔT. *Fortsch. Roentgenstrahl.*, 1950, 72: 547.

During the war period, excellent reviews on this subject appeared; however, because of the isolation there was little mutual influence to be recognized. Now, a more comprehensive treatment of the subject is possible, and here the author finds matter for astonishment in the manner in which the work in the different lands has tended to go along side by side despite the condition of isolation which has been present for so long.

For the study of pathologic conditions in the small intestine which are demonstrable roentgenologically, most of the new methods proposed for study of the small intestine can be dispensed with without great loss. The author himself still adheres to the functional diagnostic method of Weltz (*Fortschr. Roentgenstr.*, 1937, Vol. 55) and the morphological method of Pansdorf—fractionated filling—(*Fortschr. Roentgenstr.*, 1937, Vol. 56).

For the ordinary acute inflammatory conditions such as intestinal catarrh, but little has been described, aside from some acceleration of emptying, swelling of the mucosal folds, and some excess of secretion and mucus formation.

For the more subacute or chronic stages of enteritis, marked and characteristic roentgenologic signs have been related. Sclerosing and nonsclerosing forms have been depicted, that is, forms which show a tendency toward stenosis and forms which do not. Of great importance, of course, have been the studies on the bowel involved in gastrojejunal anastomoses for gastric ulcer. Here the swelling and rigidity of the walls do not need a condition of ulceration for their development. Where the edematous and congestive swelling has not progressed to a point where the surface mucosal markings are entirely erased, there results on the roentgenogram an odd appearing in-notching of the borders of the intestinal lumen, corresponding to the swollen mucosal folds. This appearance is so characteristic of the chronic enteritides of the small intestine as to be perfectly evident even to the uninitiated. This is the condition shown in Figure 2 of the original text.

Roentgen studies by the author have enabled him to construct a series of schematic representations of the successive stages in these cases of enteritis, from the condition of normal mucosal relief through the stage of edematous swelling of the mucosal folds, to the peculiar transversely striped relief herein described, and finally to the cushionlike swelling of the mucosa of such grade as to lead to the erasure of all contour markings, which is reproduced (Figure 5) in the original text. Sprue, although often considered a disease apart, in reality, gives roentgen findings which do not differ essentially from those of chronic enteritis.

Regional, terminal ileitis, or so-called Crohn's disease, is a sclerosing inflammatory process involving all the layers of the intestinal wall and leading to narrowing of the intestinal lumen and hypertrophy of the musculature, similar to the antrum gastritis and benign pyloric hypertrophy of Cruveilhier. Since it has been found that this condition by no means limits itself to the terminal ileum, but frequently passes over onto the cecum and colon, Harris, Bell, and Brunn (*Surg. Gynec. Obst.*, 1933, 57: 637) suggested that the designation be changed to that of chronic cicatrizing enteritis. The process is usually found about the lower ileum, sharply delimited from the cecum and from the proximal course of the ileum itself. The process may, however, develop at any other point in the small intestine. Most of the author's patients with regional ileitis have been anemic, though not to any great extent. The "cobblestone ileum," or nonsclerosing and nonstenosing regional ileitis described by Golden seems to be an entirely different disease, since years of close observation of these cases has failed to produce a single transition into the sclerosing form.

Enteritis necroticans was described in Germany after the first world war by Lubarsch, and this condition appeared again in the coastal regions of north Germany in 1946 and 1947. It is believed to be a result of faulty nutrition and was pronounced by Dormanns an alarming symptom of the general bad health of the population. As a rule the condition consists of an acute inflammation localizing, generally, in the upper and middle portions of the small intestine. Hemorrhages and circumscribed edematous swellings are seen in the esophagus and stomach but without necrotic changes; in the small intestines the necrosis may be extensive, leading in some cases to a discharge of the complete mucosal cast of portions of the small bowel. These changes are always arranged segmentally. Between the necrotic segments the bowel may be normal, or may exhibit hyperemic areas. The deeply penetrating necrotic processes may lead to peritonitis by contiguity, or to perforation. The eventual demarcation of the necrotic segment may lead to hemorrhage from the bowel. During the healing process polypoid masses of granulation tissue forms and the final healing shows a marked tendency to contraction and stenosis.

The roentgen findings in these cases vary with the age and grade of the process. In the acute stage (contrast media contraindicated), the appearance is that of an atonic ileus. Adequate amounts of shadow medium after the eighth to the twelfth day of the disease will disclose limited portions of the intestine without any sign of their normal peristaltic movements; the impulsive and churning movements break off shortly at this point and are picked up again at the other end. The involved portions of bowel appear to be completely stiffened and immobile. When any of the remnants of the intestinal mucosal folds are still present such structures appear to be absolutely rigid. The inter-fold recesses are narrow, frequently with the deeper end drawn out to a sharp point, and the ends of the folds themselves present an eroded appearance.

The tuberculous lesions of the small intestine are very similar to those in the large intestine. The early lesion is a tissue thickening, not an ulcerative nitching, as in the case of the gastrojejunal ulcer. Later, with the progress of the ulcerative process, the inner surface of the thickening loses its smooth character and appears eroded and indistinct in demarcation. In the earlier stages the intestinal portion assumes a mottled (polypous condition) appearance. Later the lesion loses all specific characteristics and comes to resemble the form of a stricture or tumor narrowing. Warmoes tried to make the tuberculous lesion of the small intestine susceptible of more confident recognition and pointed out the frequent concurrent involvement of the valve of Bauhin. Golden admits that the hyperplastic forms frequently cannot be differentiated from other conditions producing limited stenosis of *intestinum tenue*. Kuhlmann has pointed out the characteristics of the healed tuberculous process in the form of converging mucosal folds centering on the healed ulcerations.

New interest in the roentgenologic diagnosis of typhus began with the work of Schilling and Sametnik on the cadaver (*Fortschr. Roentgenstr.*, Vol. 43). These authors showed, by spreading shadow mixture on the flat surface of the excised bowel, that the swollen lymph glands and Peyer's patches in typhus and paratyphus could be visualized roentgenologically. The author presents two roentgenograms of portions of the small intestine in typhus showing, in one, an apparently ulcerative condition, and in the other, peculiar rounded filling defects, both exposures being of the terminal ileum.

JOHN W. BRENNAN, M. D.

The Roentgen Appearance of Thyroid Metastases in Bone. ROBERT S. SHERMAN and MORRIS IVKER. *Am. J. Roentg.*, 1950, 63: 196.

From a total of 434 cases of pathologically proved thyroid carcinoma, the authors selected 35 cases in which metastases were studied roentgenologically. In 13 of these the thyroid gland had been removed on an average of 4 years previously; 11 of the 35 patients are still living an average of 3.3 years after the appearance of bone metastases, and 2 have had metastases for periods of 7.7 and 9.5 years, respectively. The remaining 24 patients died in an average of 3 years after the appearance of metastases.

Bone metastases occurred in the following sites, and in the order of frequency given: pelvis, ribs, skull, femur, sternum, humerus, scapula. Pathologic fractures occurred in 5 of these.

A summary of the roentgen appearances is presented. Thyroid metastases in bone present the constant features of medullary origin, medullary and cortical bone destruction, and absence of periosteal reaction. Almost always the process appears oval in shape, of small to medium size, with extension to the soft parts, indistinct borders, and an essentially osteolytic internal pattern. If present at all, production takes the form of faint septa, calcific flecks, and small dense areas at the borders. A somewhat less usual feature occasionally seen is destruction in continuity. The metastases seem to be relatively radioresistant, as judged by roentgenographic studies, the slight productive changes occasionally formed not basically altering the roentgen appearance. Several case reports conclude the article.

JANE C. MACMILLAN, M.D.

The Humeral Head Defect in Recurrent Anterior Dislocation of the Shoulder. J. CRAWFORD ADAMS. *Brit. J. Radiol.*, 1950, 23: 151.

The author describes a defect in the posterolateral aspect of the articular surface of the humeral head which he considers an important factor in the production of recurrent dislocations of the shoulder. This defect has been described by other authors previously. It varies in size. The defect is a vertical groove or step which is masked and rarely seen in the direct anteroposterior radiograph. It can usually be demonstrated by internal rotation of the arm until the flexed forearm is at 60 degrees to the sagittal plane. The defect is considered to be caused by trauma; generally that violence which causes the initial dislocation probably produces a compression fracture by impingement of the humeral head against the sharp anterior margin of the glenoid. As far as the author is aware, the defect has never been demonstrated in a shoulder that has not been dislocated.

FRANK L. HUSSEY, M.D.

Death Following Angiocardiography. CHARLES T. DOTTER and FREDERICK S. JACKSON. *Radiology*, 1950, 54: 527.

In order to determine the risk involved in angiocardiography the authors attempted a survey of all centers in the United States, Canada, Great Britain, and Sweden, in which this method of examination is used. A questionnaire was sent to 1,378 general hospitals in the United States and Canada with bed capacities of 150 or more, and to all centers in Great Britain and Sweden. A reply was received from 60.7 per cent of the hospitals in the United States and Canada. The figures from Great Britain are virtually complete but those from Sweden are only partial since it was impossible to obtain information from some centers known to be using angiocardiography. The results of the survey are summarized:

TABLE I.—RESULTS OF QUESTIONNAIRE ON ANGIOCARDIOGRAPHY

Country	Centers using angiocardiography	Total no. angiocardiographic studies	Deaths reported
U.S. and Canada	150	5,961	18
Great Britain	17	413	7
Sweden*	6	450 (approx.)	1
Total	182	6,824	26

*Figures for Sweden known to be incomplete.

A second questionnaire was sent to all hospitals and centers which reported any deaths, to try to determine if possible the cause of the sudden death. The following factors were investigated: pathologic findings, dyspnea, cyanosis, vascularity of lung fields, type of contrast medium, if any sensitivity test was done, amount injected (in cubic centimeters), time of death after last injection, premedication, general anesthetic, and manner of death. The replies obtained, as regards each of these factors, are tabularly arranged by the authors for all 26 cases in which death has occurred.

In discussing their merit, 3 cases from North America are omitted since in these some other complications were also present. In 21 of the remaining 23 cases, congenital heart disease was the most important pathologic finding; 17 of these patients were cyanotic and 5 were extremely ill. The ages ranged from 12 to 51 years in 6 patients, whereas 17 were children under 8 years of age, all with congenital heart disease, 14 of whom were very cyanotic. Only one death was recorded in persons with healthy hearts, but this patient had a renal arterial disease.

In North America there was one death per 397 angiocardiograms, and in Great Britain one death per 59 angiocardiograms. The greater frequency in England is explained on the basis that the method is confined there to severe congenital heart disease; in North America it is used more widely also in conditions other than congenital heart disease.

The death occurred immediately or within 10 minutes after the injection in 8 cases, in from 15 minutes to 3 hours in 9 cases, and in from 6 hours to 3 days in 6 cases. Although in all, except one, a postmortem examination was done, the cause of death could not be determined. In about half the cases some injury to the respiratory system was suspected and in 2 cases subdural hemorrhage was found.

A study of the effect of the type of contrast medium (diodrast, pyelosil, and diodone), the number of injections, premedication, or general anesthesia revealed that these factors do not influence significantly the angiocardiographic mortality. The incidence was somewhat higher when larger doses of the contrast media were used and when the examination was done in the horizontal position. In children with congenital heart disease the incidence was the highest. T. LEUCUTIA, M.D.

RADIUM

Dosage Distribution and Dosage in Carcinoma of the Uterine Cervix. W. J. MEREDITH. *Radiology*, 1950, 54: 386.

The author describes the Manchester technique used for the treatment of carcinoma of the uterine cervix, which consists of the intracavitary application of radium tubes with or without the association of external roentgen therapy.

In applying the radium, the Paris method has been modified in order to better correlate the general radiation effect with the radiation dose. T. F. Todd demonstrated that radiation necrosis is due most commonly to a high dose in the region in which the uterine blood vessels are crossed by the ureter. This region is called the paracervical triangle.

TABLE I.—DETAILS OF LOADING AND DOSE AT POINT A

(a) Applicator loading

Vaginal ovoids	
Large (3.0 cm. diam.)	5 units each
Medium (2.5 cm. diam.)	4 " "
Small (2.0 cm. diam.)	3 " "
Intrauterine applicators (counting from fundus to cervix)	
Long (3 radium tubes)	2 2 1 units
Medium (2 radium tubes)	2 1 units
Small (1 radium tube)	2 units

(b) Dose at point "A" in 24 hours

Mgm. radium taken as unit	Roentgen dose
5	1,000
6.66	1,333
10	2,000

The author's dose system is based on due regard to the tolerance limit of the paracervical triangle. For the exact specification of the dose within the boundary of this triangle, he chooses a point which is designated as A. This point lies 2 cm. lateral to the central canal of the uterus and 2 cm. from the mucosa of the lateral fornix in the plane of the uterus. To also gain some idea of the distribution of the dose towards the pelvis a second point, designated as B, is chosen at the same level as A, but 5 cm. out.

In order to produce the desired trefoil-shaped high-dose zone, the radium is divided between a line of one, two, or three tubes in the uterus, and two applicators in the vagina—one as far out as possible in each lateral fornix. These latter, which are called ovoids, are modifications of the corks of the Paris technique. Recently they have been made of polyvinyl chloride instead of the customary hard rubber, and are used in three sizes of 2.0, 2.5, and 3.0 cm. in equatorial diameter respectively. The two ovoids are placed in the vagina either in contact or 1 cm. apart with a rubber spacer between them, thus allowing for six possible combinations.

The loads of the different applicators are expressed in terms of "units" and the dose at point A in 24 hours is given for radium sources of 5 mgm., 6.66 mgm., and 10 mgm. strength taken as a unit.

In Stages I and II radium alone is used. In Stages III and IV supplementary roentgen therapy is added to extend the high-dose zone laterally towards the point B. An eight-field technique is employed with 200 kilovolts at 40 cm. skin target distance.

The detailed procedures and the corresponding doses at points A and B are summarized in Table II.

The author noted that with this technique, if the irradiation is spread over 8 to 10 days, the uterine wall tolerates over 30,000 roentgens, the vaginal mucosa between 20,000 and 25,000 roentgens, but the rectovaginal septum breaks down after only 6,000 roentgens is given. For this reason at least

TABLE II.—TREATMENT POLICY

	Dose at		Tumor Lethal dose at:
	Point A	Point B	
Stages 1 and 2	Roentgens	Roentgens	
Radium 3 days	4,000	1,550	3.5 cm. from midline of uterus at level of A
Interval 4 days			
Radium 3 days	4,000	1,550	
Total in 10 days	8,000	3,100	
Stages 3 and 4			
Radium 3 days	3,500	1,400	5.0 cm. from midline of uterus at level of A
X-ray 24 days	2,400	3,000	
Radium 3 days	3,500	1,400	
Total in 5 weeks	9,400	5,800	

1 cm. of packing is recommended behind the ovoids to push away the sensitive tissues from the high-dose zone.

Radiation necroses, like accidents, occur in the best regulated departments. They may be the result of (a) slipped applicators, (b) retroversion of the uterus, and (c) excessive paracervical dose, although paradoxically this latter type of necrosis is often accompanied by recurrence of the carcinoma.

The present dosage levels were adopted in 1941. There has been since then a definite improvement in the 5 year survival rate which now is placed at 38 per cent. T. LEUCUTIA, M.D.

MISCELLANEOUS

Hyperthyroidism. Treatment with Radioactive Iodine. SERGEI FEITELBERG, PAUL S. KAUNITZ, SOLOMON SILVER, NORMAN SIMON, LOUIS R. WASSERMAN, and STEPHEN BENNETT YOHALEM. *Arch. Int. M.*, 1950, 85: 471.

The authors report the results obtained with radioactive iodine (I^{131}) in the treatment of 184 patients with hyperthyroidism. Of these, 150 had diffuse toxic goiter, 4 had substernal goiter, and 28 had adenomas; in 2 patients with clinical hyperthyroidism the gland could not be palpated. The diagnosis in all patients was corroborated by determination of the basal metabolic rate and by excretion tests with radioactive iodine. The size of the thyroid gland was estimated by three observers, and an initial dose, based on this estimate and on measured excretion of a tracer dose, was administered in an attempt to deliver approximately 10,000 roentgen equivalents to the gland. The average quantity of I^{131} used in these 184 patients was 8.2 millicuries, with a maximum initial dose of 11 millicuries and a minimum effective dose (after operation) of 1.7 millicuries. Doses are expressed in terms of New York millicurie. The average dose was about 10,000 roentgen equivalents, or about 80 microcuries taken up per gram of thyroid gland. In 7 cases of extremely severe disease, Lugol's solution was administered from the third to the eighteenth day after radioisotope treatment in order to accelerate a remission of symptoms.

An attempt was made to use a single therapeutic dose. Patients who were not well by clinical and laboratory criteria in 8 weeks received a second dose of radioactive iodine; only a few required a third dose. One hundred and thirty two patients were cured with a single dose of I^{131}, 43 patients required a second treatment, and 9 had three treatments. Thirteen patients developed hypothyroidism which, in all instances, was controlled by desiccated thyroid in daily doses. Since the article was submitted for publication, the authors have treated an additional 106 patients, all of whom were cured. Myxedema developed in 5. One patient required seven treatments with I^{131} (total dose, 38 microcuries).

The authors consider the use of internal radiation with I^{131} as the treatment of choice for patients with diffuse toxic goiter. In toxic adenoma its use should be reserved for those patients in whom surgical intervention is not applicable because of coincident disease which would inordinately increase the operative risk. FRANK L. HUSSEY, M.D.

MISCELLANEOUS

CLINICAL ENTITIES—GENERAL PHYSIOLOGICAL CONDITIONS

Widened Concept of Shock. Description of Local Shock (A propos des conceptions élargies du choc. La notion de choc local). X. SERAFINO. *Rev. chir.*, Par., 1950, 69: 55.

Chronic shock is characterized mainly by hypoproteinemia and diminution of the volume of the circulating blood. In addition to these two conditions, the syndrome is constituted by loss of weight, increase of extracellular fluid, and intensified susceptibility to acute shock. Neuroendocrine and metabolic inertia seem to diminish the resistance of the individual and thus create chronic shock. Protein molecules play the leading role in the physiochemical equilibrium of plasma as well as in the immunologic defense of the organism. Hence, the protein metabolism is the determining factor in the causation of conditions under discussion.

Local shock, a term introduced by Thomson and Lincoln, is characterized by local vasoconstriction followed by vasodilatation. Such a vasomotor disorder interferes with the evacuation of metabolic products deriving from the disintegration of tissues, and leads to a local anoxia. This condition produces a local fall of temperature and livid discoloration and retraction of the skin. The concept of shock has gradually been widened to include not only subacute, but also clinically asymptomatic conditions.

Visceral manifestations of a general anaphylactic disorder or those following operative trauma may serve as examples of local shock. The latter may spread and lead to generalized shock.

Vascular stasis plays an essential role in shock conditions. A zone of ischemia produced by compression of the skin, persists longer after the release of pressure in the presence of grave shock than under normal conditions. It is very doubtful, however, whether shock is always accompanied by marked disturbances of the capillary permeability. An exception is noted in local shock which appears to be accompanied by hyperpermeability of the capillaries in the affected zone.

JOSEPH K. NARAT, M.D.

Blood Volume in Surgical Disorders. W. C. WILSON. *Edinburgh, M. J.*, 1950, 57: 30.

After reviewing the methods of blood volume measurement and the recent work on hemorrhage and trauma, the author presents his experiences and the observations of other authors relative to blood volume in abdominal emergencies and surgical operations.

Four methods of estimation are described which seem to give the best claims to convenience:

1. By the carbon monoxide method, which measures directly the red cell volume, a known volume of carbon monoxide is inhaled from a closed rebreathing circuit and the blood concentration of the carbon monoxide is measured when equilibrium in the system has been reached. The total blood volume is calculated from the red cell volume and the hematocrit of the venous blood.

2. With use of the dye-hematocrit method, a known quantity of nontoxic, nondiffusable dye is injected intravenously, the dye concentration of the plasma is measured after time is allowed for mixing in the circulation, and from the dilution of the dye in the plasma the volume of plasma is calculated. With this and the hematocrit the total blood volume is calculated.

3. The differential agglutination method is ingenious. A group A subject is transfused with a known number of group O red cells, and after time is allowed for mixing, blood samples are taken. The group A red cells are agglutinated with a potent antiserum and the group O cells are counted.

4. The radioactive isotope method involves labelling red cells with radioactive iron or phosphorus, which cells are injected intravenously. Blood samples are taken at intervals afterwards, and their radioactivity is measured.

The dye-hematocrit method gives higher red cell volume than either differential agglutination or the radioactive methods, while blood volumes measured by the carbon monoxide and dye-hematocrit methods have been found to correspond quite closely. Although hemolysis and cloudiness interfere with the accuracy of the dye-hematocrit method, it is the most convenient method, especially in the investigation of acute and dangerous reduction of blood volume. The carbon monoxide is not without risk in these circumstances and the other methods are either too restricted in their application or are too complicated.

The author and his colleagues used the dye-hematocrit method (T-1824—Evans Blue), and the patients were investigated under basal conditions in the postabsorptive state. The blood samples are taken without stasis (from the femoral vein or artery when circulation is greatly depressed) and at 10, 20, and 30 minutes after injection. Plasma dye concentrations are determined by the use of a photoelectric absorptiometer. For routine clinical work, a simpler method of taking a single sample at 10 minutes after the injection and the hematocrit is determined from the hemoglobin or specific gravity estimations. This involves an average error of from 1.3 per cent to 3.3 per cent.

After small bleedings dilution begins as early as 30 minutes, and may be well advanced at 2 hours, but is usually not complete until 24 hours. Not infrequently, over-dilution occurs. Generally speaking, dilution is a slow process in man. There is no evidence that any significant number of red cells is

added to the circulation. When a liter or more of blood is withdrawn, completion of dilution is still further delayed. Hemorrhagic "shock" occurs following the loss of 30 to 50 per cent of the blood volume. Failing transfusion, profound and progressive changes in the tissue oxidation and oxygen consumption, severe acidosis, and other features of stagnant anoxia supervene. The central feature of traumatic "shock" is reduced blood volume, due entirely to hemorrhage. There is no generalized increase in capillary permeability. Hemoconcentration occurs only when plasma is lost, as in burns, and plasma loss is confined to the site of injury. Whether prolongation of the period of anoxia can produce a state irremediable by transfusions is undecided.

Severe trauma often proves fatal, although hemorrhage is controlled and blood volume is fully restored and maintained, as in injuries to the brain and lungs and injuries complicated by massive bacterial infection or fat embolism. Abdominal injury may be followed by complex circulatory disturbances and may be fatal within a few hours. The majority of the fatalities, however, are due to renal failure several days later.

Apparently, injury involving a large reduction in blood volume is followed by active renal vasoconstriction which persists long after the blood volume and cardiac output have been restored. Renal failure is more common after abdominal than after limb wounds. Similar changes are found in peritonitis.

Common changes in peritonitis are a reduction in blood volume, mainly of plasma volume, a parallel reduction of total circulating protein, and a disproportionate fall of the total circulating albumin. There is evidence of impaired liver and renal function. Liver function is quickly restored but the kidney function remains disturbed for days. In patients who recover, the volume and protein deficits are speedily corrected by intravenous infusions, except that of the total circulating albumin, which may persist for weeks. Sometimes the cell volume declines from the fourth day, for 2 weeks or longer.

Plasma volume reduction in peritonitis seems to be due to plasma exudation in the zone of inflammation, or to ileus with large fluid and salt losses. Sometimes both are present. Early decline in cell volume may be due to stagnation—possibly at the zone of inflammation—and the later slow decline due, in part, to extravasation and loss of cells into the lumen and wall of the inflamed and obstructed bowel.

There seems to be some adaptation to the reduced blood volume when peritonitis develops slowly. This adaptation, however, is less striking than in severe anemia.

Oligemia, or failure of adaptation to it, and bacterial intoxication contribute to the final collapse of patients.

Simple fluid depletion can be followed by striking circulatory and renal disturbances.

TABLE I.—BLOOD LOSS IN OPERATIONS

Operations	Cases	Blood loss in ml.		
		Max.	Min.	Av.
Herniotomy	4	40	15	27
Gastrojejunostomy	2	100	62	81
Lumbar sympathectomy	4	122	78	94
Resection of intestine or colon	4	420	80	230
Total gastrectomy. Splenectomy, partial pancreatectomy	1	323	...	....
On bile passages	5	1023	45	381
Brain—acoustic neuroma	1	476	...	....
Radical mastectomy	10	968	374	546
Partial gastrectomy	9	1273	157	559
Splenectomy	3	923	280	614
Bone tumors	3	865	500	730
Perineal excision of rectum	2	1090	948	1019
Abdominoperineal excision of rectum, etc.	10	1748	581	1140
Total	58	....	...	....

Simple occlusion of the bowel and strangulation of small segments is associated with a fall of plasma volume only when fluid and salt losses have been large. Strangulation of larger segments is followed by pronounced reduction in plasma and cell volumes. In the early stage the fall is easily corrected by transfusion of blood, but in the late stages when the bowel has lost, or is losing, its viability the response to treatment is similar to that in severe peritonitis. The author believes it is better to resect doubtfully viable bowel in every case.

TABLE II.—BLOOD LOSS AND BLOOD VOLUME

Case	Sex and age	Operation	Duration min.	B.P. fall.	Blood loss		Volume changes	
					ml.	Per cent B.V.	Plasma	Blood
A	F. 60	Laparotomy	30	Nil	55	2	+163	+157
B	F. 47	Cholecystectomy	80	Nil	45	1	+408	+506
C	F.64	Radical mastectomy	90	Small	477	14	−321	−433
D	M. 51	Partial gastrectomy	120	Large	877	18	−875	−1091
E	M. 67	Abdominoperineal excision of rectum	167	Large	965	24	−317	−639
F	M. 71	Abdominoperineal excision of rectum	150 (115)*	Large	1125	20	−900	−1607
G	M. 69	Abdominoperineal excision of rectum	135 (110)*	Large	1514	27	−1270	−2510

*Figs. in brackets = time of blood volume estimation.

Blood loss occurring during operation varies greatly. Loss of a liter or more during a prolonged operation produces intense shock, and when the loss reaches 1,200 milliliters the blood pressure often becomes unrecordable and the radial pulse impalpable.

Blood volume estimations after large blood losses are not entirely reliable and may be too low, although in the majority of cases there is a reasonably good correspondence. With large blood losses the volume fall tends to be greater than the blood loss. If the discrepancy between blood loss and blood volume fall is a real one it would indicate that during severe operations a fraction of the blood stagnates and passes out of effective circulation; thus the danger to life would be disproportionate to the quantity of blood lost.

Hemorrhage during operation is more serious than that in a conscious patient. Transfusion is always desirable after a loss of 800 milliliters to a liter of blood, and it becomes imperative after the loss of 1,200 or more milliliters of blood. Anesthetic drugs, particularly ether and the barbiturates, render the patient more sensitive to blood loss. Repeated small bleedings are less well tolerated than single large bleeding of the same volume. The indications are that the responses of the small blood vessels are altered, whereby the flow of blood in the peripheral circulation is greatly retarded.

Cases are reported to illustrate the points made.

JACOB T. BRADSHER, M.D.

Contribution to the Subject of the Cushing Syndrome (Beitrag zum Cushing-Syndrom). WERNER CATEL. *Neue med. Welt.*, 1950, 1: 83.

A series of 5 photographs are presented in the original text. The first picture shows a slender handsome boy of 9 years, with a thin, intelligent-looking face. The second picture shows the Cushing syndrome already well developed. The condition started to develop shortly after the age of 10 years. The photograph taken at 14.5 years exhibits the full blown syndrome with the moon-shaped face, enormously fat trunk with the typical purpural striae, kyphosis, hypertrichosis, and relatively slender limbs.

At this most advanced stage of the disease the boy was bedridden because of weakness and lumbar pain, and perhaps also because of a marked mental and emotional apathy. There was present a hyperglycemia (particularly marked with the glucose tolerance test), hypertension, hypercholesterinemia, and a mild grade of hypercalcemia. The roentgen examination disclosed a more or less generalized osteoporosis, particularly marked in the spinal column where the vertebral bodies exhibited in the thoracic and lumbar regions a marked decrease in calcium content, narrowed bodies, and irregular epiphyseal lines. The skull bones were thinned, but the sella turcica was normal in appearance.

Roentgen therapy was given, at first to the hypophyseal region and later to the suprarenal glands, without apparent benefit. The left suprarenal gland was then removed; removal was followed by rapid and continued improvement, so that the photograph of the young man at 17.5 years of age disclosed a perfectly built youth with normal sexual development. He then seemed to be in perfect health and was able to perform heavy labor without inconvenience.

Histologic examination of the removed suprarenal gland in serial sections failed to bring to light an adenoma, or other gross pathological changes in the gland substance. There was an almond-sized hemorrhage in the region between the innermost cortical layer and the medullary substance. The borders of this cavity showed in places a bloody discoloration, and the bordering cortical and medullary layers exhibited a dirty dark-red discoloration. Transverse sections showed that the hemorrhagic cavity extended through the entire upper half of the suprarenal gland and as far in depth as the large medullary veins. The cortex was, as a whole, intensely yellow in color, and the medulla exhibited a grayish discoloration. The venous sinuses and the veins of the inner cortical zone and of the medulla were markedly distended with blood. The hematoma may have been produced during the operation itself.

The author believes that the syndrome was the result of faulty functioning of the suprarenal glands operating directly on the body metabolism, or indirectly on the other organs of internal secretion. Thus, the hormone of the cortex of the suprarenals might affect directly the phosphorization in the intestinal wall with results on the carbohydrate and vitamin metabolism, or might affect the protein and fat metabolism as a result of stimulating the process of ketone production, and might affect the excretion of sodium chloride and the metabolism of the other minerals. The hyperglycemia would, on the other hand, be the result of stimulation of the pancreas; the osteoporosis and hypercalcemia the result of the stimulation of the epithelial bodies; and the hypertension the result of the stimulation of the chromaffin system. The obesity might also be a secondary manifestation, resulting from stimulation of the diencephalohypophyseal region.

Unfortunately the preoperative biologic or colorimetric study of the urinary excretion of dehydroandrosterone could not be done.

JOHN W. BRENNAN, M.D.

The Possibilities in the Cytologic Diagnosis of Cancer (Die Moeglichkeiten einer zytologischen Krebsdiagnostik). HERMANN HENGSTMANN. *Neue med. Welt.*, 1950, 1: 224.

A disadvantage of the cytologic method of diagnosis, in any form, is that it gives purely a positive result; cancer cannot be ruled out. Another disadvantage lies in the fact that despite the efforts of numerous scholars there has been produced no single characteristic of the cancer cell which distinguishes it from all others. The most distinguishing characteristic of cancer cells in general is their polymorphism as observed when they are present together in large numbers.

In the various fluids and secretions the tumor cells appear singly or in cell groups or complexes; however, actual tumor stroma is but rarely encountered. Therefore, the term cytohistology (Richardson and coworkers, *Am. J. Clin. Path.*, 1949, 19: 323, 328), is, in the author's opinion, fraught with the possibility of misunderstanding and error when used diagnostically.

In order to procure material as free from contamination and as fresh as possible, that author has developed the so-called "aimed puncture" method. This consists in introducing a 2 mm. cannula with an accurately fitting mandrin and a cylindrical square-ground point into, or as near as possible to, the tumor mass, metastasis, or lymph node and procuring by suction a small cylinder of tissue which may then be examined on a smear or daub preparation. This method may be correlated with the findings procured by examination of the desquamated contents of the body fluids and secretions. Also, when possible, biopsy and surgical specimens must be procured to check against the cytological findings, at least until such time as the latter can be placed on a firmer basis. The author believes that for the interpretation of the cytologic specimens, previous training of the cytologist in pathology would be of value; he believes this to be true despite the claims of Papanicolaou who states that the lack of such training enables the cytologist to approach the examination with a more open mind.

The results reported in America with the cytologic method seem better than those reported in Germany, perhaps because in America there are good schools for the training of cytologists while in Germany the examination is frequently made by the clinician. The examiner should, of course, be thoroughly schooled, not only in the recognition of the characteristics of the tumor cell, or cell agglomerations, but also in the normal cytology of the region under study, so that the atopic character of the neoplastic cell can be spotted almost automatically. In this training of the cytologist the tissue removed at operation or autopsy should be available for comparison with the other findings.

The staining methods of May-Gruenwald and Giemsa are regarded as the best for general examination, although the excellencies of the method of Papanicolaou are acknowledged. The phase-contrast procedure in which the fresh, living cell free of secondary changes is observed, is mentioned; it is recognized as an advance, but is not especially new.

JOHN W. BRENNAN, M.D.

Presentation of the Results of Cancer Treatment. RALSTON PATERSON and MARGARET TOD. *Brit. J. Radiol.*, 1950, 23: 146.

No generally accepted method of providing dependable statistics from which the results of cancer treatment may be assessed is at present available. The authors present certain working principles that they consider essential for the uniform presentation of the results of this treatment.

These principles include (1) simplicity, (2) the showing of all relevant figures, (3) an agreed method of presenting percentage results, preferably by the crude survival percentage which takes the number of known alive over the total number in the sample, and (4) agreed fixed reporting periods, conveniently at the third, fifth and tenth years.

Examples of tables (using crude rates) are given, and suggestions are made for improved control by preregistration. An audit was carried out before publication of the statistical reports.

ELY ELLIOTT LAZARUS, M.D.

Treatment of Lymphosarcoma of the Neck by a Combination of Nitrogen-Mustard Therapy, Roentgen Therapy, and Surgery (Traitement d'un lymphosarcome du cou par l'association du nitrogène-moutarde de la radiothérapie et de la chirurgie). F. CABY and H. TSEVRENIS. *Presse méd.*, 1950, 58: 410.

A 39 year old male noted enlargement of the cervical lymph nodes on the right side some 3 weeks before coming in for consultation. The patient was thin, suffered some pain irradiating into the right hemithorax, and had a subfebrile temperature. Puncture of an enlarged gland resulted in a diagnosis of primary lymphosarcoma of the neck. The cells were immature, the protoplasm was intensely basophilic, and the nuclei were reticular and contained nucleoli. The cells tended to be atypical and recalled the basophilic erythroblasts of the bone marrow. Nitrogen-mustard, associated with atropin (yperite) was initiated in daily oral doses of 5 mgm. for 5 days without serious inconvenience to the patient. This resulted in a spectacular melting away of the enlarged nodes without, however, complete disappearance.

Surgical evacuation of the area was then practiced, and during the entire further course of the disease there was no further evidence of activity in this area. However, a month later the deeper glands of the right side began to enlarge, together with the superficial glands of the left side. Further courses of nitrogen-mustard resulted in the retreat of the process on the left side, but merely arrested (after a total of 45 mgm. of yperite) that on the right.

The addition of roentgen therapy resulted in a temporary recession of the process on the right side; however, after 1.5 months a recurrence appeared in the carotid glands on the right side. This time neither nitrogen-mustard nor huge doses of roentgen rays had more than a temporary arresting effect and removal of the right carotid chain of nodes was undertaken surgically as a last recourse. During this operation the jugular vein system was opened twice and some air was sucked into the heart, without, however, any apparent ill effects. The operation was quite bloody and was terminated with a blood transfusion. This transfusion corrected a tendency toward leucopenia (apparently a result of the nitrogen-mustard therapy).

A month after this last operation a new recurrence developed as a rapid generalization of the sarcoma-

tous process. A mass appeared in the mediastinum, the lymph nodes in both axillae enlarged, and edema appeared in the right upper extremities. A course of 15 mgm. of nitrogen-mustard caused a disappearance of the edema; however, the patient died 6.5 months after the first examination.

As a result of this experience the authors' advice for this type of case is surgical exeresis of the affected nodes after a preliminary attack with yperite combined with roentgen therapy.

JOHN W. BRENNAN, M.D.

DUCTLESS GLANDS

Thyroinhibitive Action of Thiocyanate of Potassium and of Propylthiouracil (L'action thyroinhibitrice du thiocyanate de potassium et du propylthiouracil). G. H. DELTOUR and D. HIOCO. *Ann. endocr.*, Par., 1949, 10: 411.

A series of albino rats were given increasing doses of N-propylthiouracil for 10 days. The weight of the thyroid gland per 100 gm. of body weight of the animal increased from 21.5 to 70 mgm. and the iodine content of the thyroid gland tissue rapidly disappeared. Thiocyanate of potassium used in the same manner produced much less hyperplasia of the gland and a far smaller decrease in its iodine content.

Two other series of white rats were given the usual de-iodinizing 10 day injections, the one with N-propylthiouracil and the other with thiocyanate of potassium. However, they were given, in addition, increasing doses of iodide of potassium. With the large doses applied neither of the antithyroid preparations were able to prevent a certain amount of iodine fixation by the thyroid gland.

A series of these experimental animals were de-iodinized in the usual manner, being given 5 mgm. per 100 gm. of body weight of the thiouracil for 10 days. Each of the animals was then given 1 mgm. of potassium thiocyanate, and this injection was followed at lengthening intervals by the subcutaneous injection of potassium iodide. The subsequent analyses of these glands showed that the effects of the injection of potassium thiocyanate did not last longer than 5 hours. When the propylthiouracil was simply discontinued after the de-iodinizing 10 day treatment, without the addition of any other medication, the weight of the gland returned to normal within 10 days and the iodine content not only returned to normal but even surpassed the normal.

A series of white rats, de-iodinized as described, received during the last 3 days of the 10 day course of thiouracil varying dosages of potassium iodide and potassium thiocyanate as the authors wished to determine the amount of potassium iodide required to neutralize the antithyroid effects of a given amount of potassium thiocyanate. It was found that approximately one-half milligram of potassium iodide was sufficient to neutralize the effects of 30 mgm. of potassium thiocyanate.

In a final experimental series the authors attempted to determine the point in the absorption and metabolism of iodine by the thyroid gland at which the effects of the potassium thiocyanate are exerted. The animals were de-iodinized as described, and then 90 minutes before death each received 1 mgm. of potassium iodide. This was followed in 30 minutes (1 hour before death) by increasing amounts of the thiocyanate of potassium. It was found that the thiocyanate not only prevented the absorption of any new amounts of iodine but actually removed some which had become fixed during the previous 30 minutes. This is regarded as a further argument in favor of the theory that the action of the potassium iodide affects the absorption of inorganic iodine by the thyroid, but has no effect on the iodine of this organ once it has undergone organic synthesis (thyroxine, di-iodotyrosine).

From these studies the authors conclude that potassium thiocyanate has no appreciable antithyroid effect when limited to physiologic quantities.

JOHN W. BRENNAN, M.D.